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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	May 12	EXTEND option available in structure searching
NEWS 4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 5	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS 6	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS 7	Jun 28	Additional enzyme-catalyzed reactions added to CASREACT
NEWS 8	Jun 28	ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG, and WATER from CSA now available on STN(R)
NEWS 9	Jul 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 10	Jul 30	BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting
NEWS 11	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 12	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 13	AUG 02	STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting
NEWS 14	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 15	AUG 04	Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004
NEWS 16	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 17	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 18	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 19	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 20	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 21	SEP 14	STN Patent Forum to be held October 13, 2004, in Iselin, NJ

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:38:27 ON 15 SEP 2004

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 10:38:42 ON 15 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 SEP 2004 HIGHEST RN 744786-72-9
DICTIONARY FILE UPDATES: 14 SEP 2004 HIGHEST RN 744786-72-9

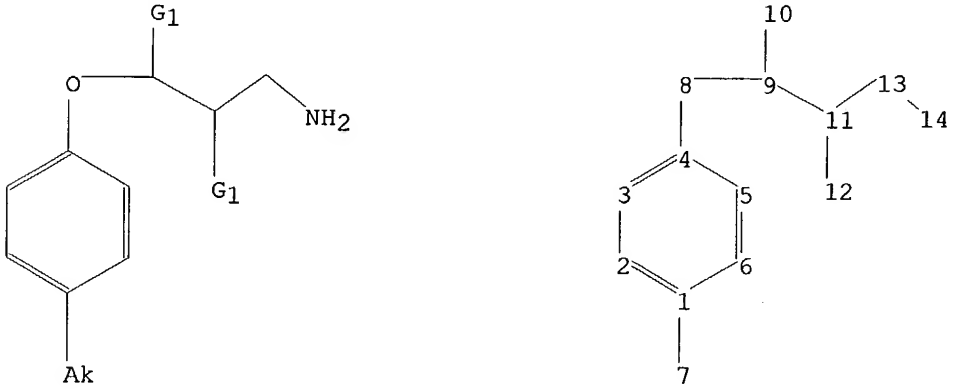
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10032266.str



chain nodes :
7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6
chain bonds :
1-7 4-8 8-9 9-10 9-11 11-12 11-13 13-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-7 4-8 8-9 9-10 11-12 13-14

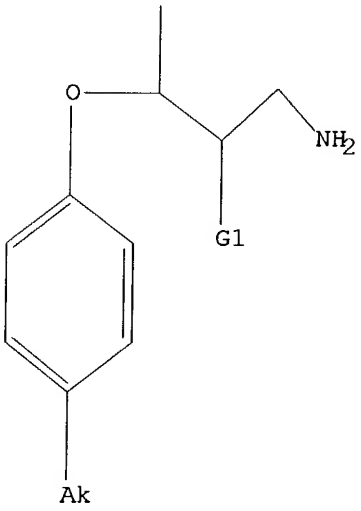
exact bonds :
9-11 11-13
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:H,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
 11:CLASS 12:CLASS 13:CLASS 14:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

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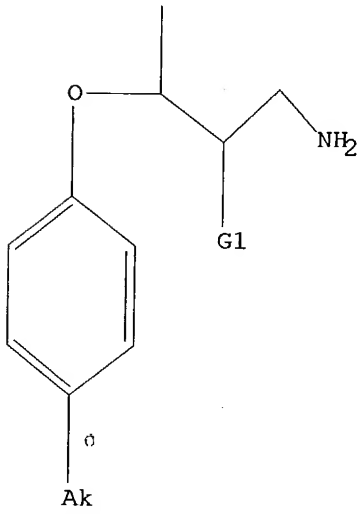
L1 HAS NO ANSWERS
L1 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

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=> s l1 sss sam
SAMPLE SEARCH INITIATED 10:40:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   8251 TO ITERATE

 12.1% PROCESSED    1000 ITERATIONS                                 8 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       159577 TO   170463
PROJECTED ANSWERS:             833 TO     1807

L2             8 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 10:40:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 164247 TO ITERATE

100.0% PROCESSED  164247 ITERATIONS                              689 ANSWERS
SEARCH TIME: 00.00.03

L3           689 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             156.68     156.89

FILE 'CAPLUS' ENTERED AT 10:41:02 ON 15 SEP 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 15 Sep 2004 VOL 141 ISS 12
FILE LAST UPDATED: 14 Sep 2004 (20040914/ED)

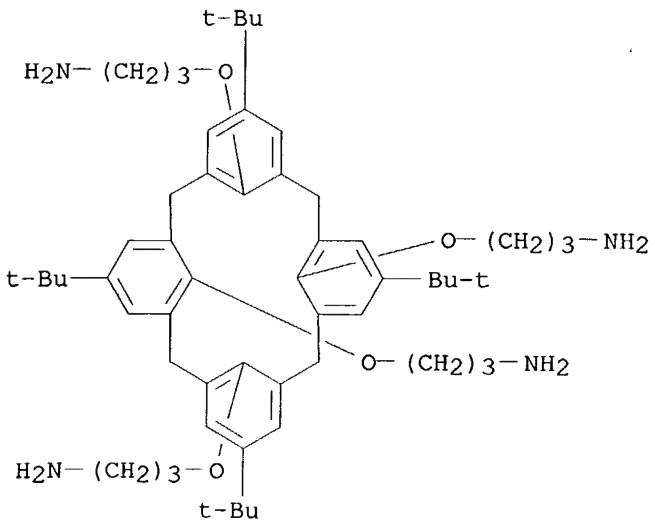
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 872 L3

=> s l4 and fuel
338411 FUEL
154440 FUELS
387188 FUEL
(FUEL OR FUELS)
L5 2 L4 AND FUEL

=> d l5 hitstr, ibib, iabs 1-2

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
IT **226998-70-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and condensation with phosphinylacetic acid ester)
RN 226998-70-5 CAPLUS
CN 1-Propanamine, 3,3',3'',3'''-[[5,11,17,23-tetrakis(1,1-dimethylethyl)pentacyclo[19.3.1.13,7.19,13.115,19]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene-25,26,27,28-tetrayl]tetrakis(oxy)]tetrakis- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 2000:368368 CAPLUS
DOCUMENT NUMBER: 133:17635
TITLE: Preparation of ((phosphinylacetyl)amino)alkoxy-substituted calixarenes and their use in extracting

actinides and lanthanides

INVENTOR(S): Dozol, Jean-francois; Garcia Carrera, Alejandro; Bohmer, Volker; Matthews, Susan E.

PATENT ASSIGNEE(S): Commissariat a l'Energie Atomique, Fr.

SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2

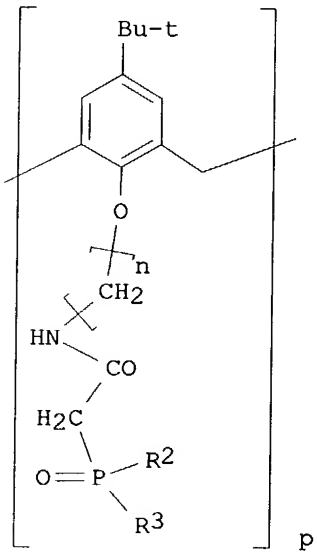
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031087	A1	20000602	WO 1999-FR2893	19991124
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2786487	A1	20000602	FR 1998-14902	19981126
FR 2786487	B1	20010105		
EP 1133501	A1	20010919	EP 1999-956134	19991124
EP 1133501	B1	20030212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002540061	T2	20021126	JP 2000-583915	19991124
ES 2192090	T3	20030916	ES 1999-956134	19991124
US 6657081	B1	20031202	US 2001-831921	20010529

PRIORITY APPLN. INFO.: FR 1998-14902 A 19981126
WO 1999-FR2893 W 19991124

OTHER SOURCE(S): CASREACT 133:17635; MARPAT 133:17635

GRAPHIC IMAGE:



ABSTRACT:
((Phosphinylacetyl)amino)alkoxy-substituted calixarenes (I; R1 = alkyl, aryl, H; R2 and R3, identical or different, = alkyl or aryl; n = 2-8; p = 4-8) and method of preparation are claimed. The preparation involves condensation of (aminoalkoxy)calixarenes with R2R3P(O)CH2CO2R4 (R4 = p-nitrophenyl, 2,4-dinitrophenyl). The (aminoalkoxy)calixarenes were prepared from hydroxycalixarenes and N-(bromoalkyl)phthalimides followed by reaction with

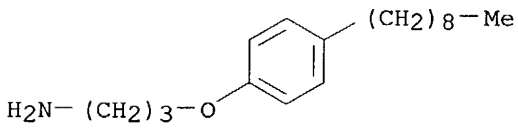
hydrazine; alternatively, for n = 2, hydroxycalixarenes were reacted with alkyl bromoacetates to give esters that were reduced to alcs., which were converted to tosylates, which were reacted with sodium azide followed by catalytic hydrogenation. Data are given for the use of said calixarenes for extracting actinides and lanthanides from aqueous solns. into hexyl o-nitrophenyl ether. The distribution coeffs. for the claimed calixarenes are much greater than those for the comparison extractant, Ph2P(O)CH2C(O)NiBu2. These extractants may be useful for processing aqueous effluents coming from used nuclear **fuel** retreatment installations.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
IT **39611-60-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 39611-60-4 CAPLUS
CN Phosphoric acid, dioctyl ester, compd. with 3-(4-nonylphenoxy)-1-propanamine octyl phosphate (2:3:2) (9CI) (CA INDEX NAME)

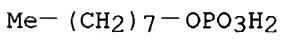
CM 1

CRN 47096-69-5
CMF C18 H31 N O



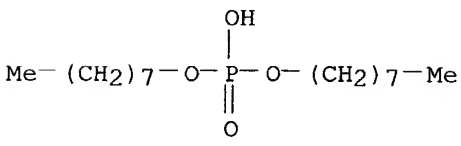
CM 2

CRN 3991-73-9
CMF C8 H19 O4 P



CM 3

CRN 3115-39-7
CMF C16 H35 O4 P



ACCESSION NUMBER: 1973:29410 CAPLUS
DOCUMENT NUMBER: 78:29410
TITLE: 3-Phenoxypropylamine-alkyl phosphate additives for motor **fuels**
INVENTOR(S): Haemmerle, Bernard; Sillion, Bernard; De Gaudemaris, Gabriel

PATENT ASSIGNEE(S): Institut Francais du Petrole, des Carburants et Lubrifiants; Entreprise de Recherches et d'Activites Petrolieres (ELF)
SOURCE: Fr., 6 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2105539		19720602	FR 1970-32971	19700910

GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
The phenoxypropylamine addition compound I, useful as a **fuel** detergent, is prepared from p-nonylphenol in a series of reactions. The ether, p-C9H19C6H4O(CH2)2CN, is prepared by acrylonitrile addition and hydrogenated to p-C9H19C6H4O(CH2)3NH2. The amine reacts with an equimolar mixture of C8H17OP(O)(OH)2 and (C8H17O)2P(O)OH to give I.

```
=> s l4 and (polyalkyl or polyisobutyl or polyisobutene)
          1653 POLYALKYL
             8 POLYALKYLS
          1660 POLYALKYL
                 (POLYALKYL OR POLYALKYLS)
           359 POLYISOBUTYL
          1955 POLYISOBUTENE
           121 POLYISOBUTENES
          1993 POLYISOBUTENE
                 (POLYISOBUTENE OR POLYISOBUTENES)
L6           0 L4 AND (POLYALKYL OR POLYISOBUTYL OR POLYISOBUTENE)

=> s l4 and (gas?)
       1845556 GAS?
L7           47 L4 AND (GAS?)

=> d l7 1-47 all

L7   ANSWER 1 OF 47  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:633436  CAPLUS
DN   141:174191
ED   Entered STN:  06 Aug 2004
TI   Preparation of pyrazolopyrimidines as a small conductance potassium
     channel (SK channel) blocking agents
IN   Takamuro, Iwao; Sekine, Yasuo; Tsuboi, Yasunori; Nogi, Kouji; Taniguchi,
     Hiroyuki
PA   Tanabe Seiyaku Co., Ltd., Japan
SO   PCT Int. Appl., 306 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  A61K
CC   28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1, 63
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ----------          ----   --------    --------------------     --------
PI   WO 2004064721        A2    20040805    WO 2004-JP617            20040123
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
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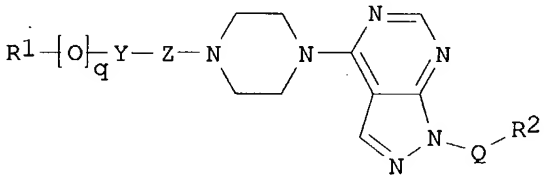
CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
IS, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR,
LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ,
NA, NI, NI, NO

PRAI JP 2003-16770 A 20030124
JP 2003-205341 A 20030801
JP 2003-385399 A 20031114

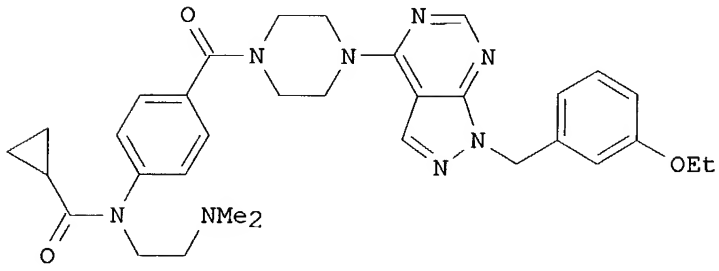
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004064721	ICM	A61K

GI



I



II

AB The title compds. [I; R1 = substituted aryl, (un)substituted nitrogen-containing aliphatic heteromonocyclyl, substituted cycloalkyl, (un)substituted amino, or substituted heteroaryl; R2 = (un)substituted (hetero)aryl; Y = a single bond, alkylene or alkenylene; Z = CO, CH2, SO2, C:N(CN); Q = alkylene; q = 0-1] and their pharmaceutically acceptable salts, which have a small conductance potassium channel (SK channel) blocking activity, were prepared Thus, treating Et 4-{N-(cyclopropylcarbonyl)-N-[2-(dimethylamino)ethyl]amino}benzoate (preparation given) with 2N NaOH solution followed by treatment with 2N HCl, and the reaction of the resulting acid with 1-(3-ethoxybenzyl)-4-(piperazin-1-yl)-1H-pyrazol[3,4-d]pyrimidine dihydrochloride afforded 84% II which showed an excellent apamin-binding inhibitory activity (IC50 of 0.05 μM). The pharmaceutical composition comprising the compound I is claimed.

ST pyrazolopyrimidine prepn small conductance potassium channel SK blocker

IT Intestine, disease
(constipation, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Mental disorder
(depression, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Learning
Memory, biological
(disorder, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Digestive tract, disease
(**gastroesophageal** reflux, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Intestine, disease
(ileus, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Intestine, disease
(irritable bowel syndrome, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Muscular dystrophy
(myotonic, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Ion channel blockers
(potassium; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Anti-Alzheimer's agents
Antidepressants
Cognition enhancers
Laxatives
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Apnea
(sleep apnea, treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT Alzheimer's disease
(treating; preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 733770-28-0P 733774-83-9P 733774-87-3P 733774-88-4P 733774-96-4P
733775-29-6P 733778-35-3P 733782-46-2P 733782-48-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 733770-06-4P 733770-07-5P 733770-08-6P 733770-09-7P 733770-11-1P
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733770-34-8P 733770-35-9P 733770-36-0P 733770-37-1P 733770-38-2P
733770-40-6P 733770-42-8P 733770-44-0P 733770-46-2P 733770-48-4P
733770-49-5P 733770-50-8P 733770-51-9P 733770-52-0P 733770-53-1P
733770-54-2P 733770-55-3P 733770-56-4P 733770-57-5P 733770-58-6P
733770-59-7P 733770-60-0P 733770-61-1P 733770-62-2P 733770-63-3P
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733770-69-9P 733770-70-2P 733770-71-3P 733770-72-4P 733770-73-5P
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733770-99-5P 733771-00-1P 733771-01-2P 733771-02-3P 733771-03-4P
733771-04-5P 733771-06-7P 733771-08-9P 733771-10-3P 733771-12-5P
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733771-79-4P 733771-80-7P 733771-81-8P 733771-82-9P 733771-83-0P
733771-84-1P 733771-85-2P 733771-87-4P 733771-88-5P 733771-89-6P
733771-90-9P 733771-91-0P 733771-92-1P 733771-93-2P 733771-94-3P
733771-95-4P 733771-96-5P 733771-97-6P 733771-98-7P 733771-99-8P
733772-00-4P 733772-01-5P 733772-02-6P 733772-03-7P 733772-04-8P
733772-05-9P 733772-06-0P 733772-07-1P 733772-08-2P 733772-09-3P
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733772-15-1P 733772-16-2P 733772-17-3P 733772-18-4P 733772-19-5P
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733772-25-3P 733772-26-4P 733772-27-5P 733772-28-6P 733772-29-7P
733772-30-0P 733772-31-1P 733772-32-2P 733772-33-3P 733772-34-4P
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733772-45-7P 733772-46-8P 733772-47-9P 733772-48-0P 733772-49-1P
733772-50-4P 733772-51-5P 733772-52-6P 733772-53-7P 733772-54-8P
733772-55-9P 733772-56-0P 733772-57-1P 733772-58-2P 733772-59-3P
733772-60-6P 733772-61-7P 733772-62-8P 733772-63-9P 733772-64-0P
733772-65-1P 733772-66-2P 733772-67-3P 733772-68-4P 733772-69-5P
733772-70-8P 733772-71-9P 733772-72-0P 733772-73-1P 733772-74-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 733772-75-3P 733772-76-4P 733772-77-5P 733772-78-6P 733772-79-7P
733772-80-0P 733772-82-2P 733772-84-4P 733772-86-6P 733772-87-7P
733772-88-8P 733772-89-9P 733772-92-4P 733772-95-7P 733772-98-0P
733772-99-1P 733773-02-9P 733773-04-1P 733773-06-3P 733773-08-5P
733773-10-9P 733773-12-1P 733773-14-3P 733773-16-5P 733773-18-7P
733773-20-1P 733773-22-3P 733773-24-5P 733773-26-7P 733773-28-9P
733773-30-3P 733773-32-5P 733773-34-7P 733773-36-9P 733773-38-1P
733773-40-5P 733773-42-7P 733773-44-9P 733773-46-1P 733773-48-3P
733773-50-7P 733773-52-9P 733773-53-0P 733773-55-2P 733773-57-4P
733773-59-6P 733773-60-9P 733773-61-0P 733773-62-1P 733773-63-2P
733773-64-3P 733773-65-4P 733773-67-6P 733773-68-7P 733773-69-8P
733773-70-1P 733773-71-2P 733773-72-3P 733773-73-4P 733773-74-5P
733773-75-6P 733773-76-7P 733773-77-8P 733773-78-9P 733773-79-0P
733773-80-3P 733773-81-4P 733773-82-5P 733773-83-6P 733773-84-7P
733773-85-8P 733773-86-9P 733773-87-0P 733773-88-1P 733773-89-2P
733773-90-5P 733773-91-6P 733773-92-7P 733773-93-8P 733773-94-9P
733773-95-0P 733773-96-1P 733773-97-2P 733773-98-3P 733773-99-4P
733774-00-0P 733774-01-1P 733774-02-2P 733774-03-3P 733774-04-4P
733774-05-5P 733774-06-6P 733774-07-7P 733774-08-8P 733774-09-9P
733774-10-2P 733774-11-3P 733774-12-4P 733774-13-5P 733774-14-6P
733774-15-7P 733774-16-8P 733774-17-9P 733774-18-0P 733774-19-1P
733774-20-4P 733774-21-5P 733774-22-6P 733774-23-7P 733774-24-8P
733774-25-9P 733774-26-0P 733774-27-1P 733774-28-2P 733774-29-3P
733774-30-6P 733774-31-7P 733774-32-8P 733774-33-9P 733774-34-0P
733774-35-1P 733774-36-2P 733774-37-3P 733774-38-4P 733774-39-5P
733774-40-8P 733774-41-9P 733774-42-0P 733774-43-1P 733774-44-2P
733774-45-3P 733774-46-4P 733774-47-5P 733774-48-6P 733774-49-7P
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733774-60-2P 733774-61-3P 733774-62-4P 733774-63-5P 733774-64-6P
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733774-70-4P 733774-71-5P 733774-72-6P 733774-73-7P 733774-74-8P
733774-75-9P 733774-76-0P 733774-77-1P 733774-78-2P 733774-79-3P
733774-80-6P 733774-81-7P 733774-82-8P 733774-85-1P 733774-86-2P
733774-90-8P 733774-92-0P 733774-94-2P 733774-97-5P 733774-99-7P
733775-01-4P 733775-03-6P 733775-05-8P 733775-07-0P 733775-09-2P
733775-10-5P 733775-11-6P 733775-12-7P 733775-13-8P 733775-14-9P
733775-15-0P 733775-16-1P 733775-17-2P 733775-18-3P 733775-19-4P
733775-20-7P 733775-21-8P 733775-22-9P 733775-23-0P 733775-24-1P

733775-25-2P 733775-26-3P 733775-27-4P 733775-28-5P 733775-30-9P
733775-31-0P 733775-32-1P 733775-33-2P 733775-34-3P 733775-35-4P
733775-36-5P 733775-37-6P 733775-38-7P 733775-39-8P 733775-40-1P
733775-41-2P 733775-42-3P 733775-43-4P 733775-44-5P 733775-45-6P
733775-46-7P 733775-49-0P 733775-50-3P 733775-51-4P 733775-52-5P
733775-53-6P 733775-54-7P 733775-55-8P 733775-56-9P 733775-57-0P
733775-58-1P 733775-59-2P 733775-60-5P 733775-61-6P 733775-62-7P
733775-63-8P 733775-64-9P 733775-65-0P 733775-66-1P 733775-67-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 733775-68-3P 733775-69-4P 733775-70-7P 733775-71-8P 733775-72-9P
733775-73-0P 733775-74-1P 733775-75-2P 733775-76-3P 733775-77-4P
733775-78-5P 733775-79-6P 733775-80-9P 733775-81-0P 733775-82-1P
733775-83-2P 733775-84-3P 733775-85-4P 733775-86-5P 733775-87-6P
733775-88-7P 733775-89-8P 733775-90-1P 733775-91-2P 733775-92-3P
733775-93-4P 733775-94-5P 733775-95-6P 733775-96-7P 733775-97-8P
733775-98-9P 733775-99-0P 733776-00-6P 733776-01-7P 733776-02-8P
733776-03-9P 733776-04-0P 733776-05-1P 733776-06-2P 733776-07-3P
733776-08-4P 733776-09-5P 733776-10-8P 733776-11-9P 733776-12-0P
733776-13-1P 733776-14-2P 733776-15-3P 733776-16-4P 733776-17-5P
733776-18-6P 733776-19-7P 733776-20-0P 733776-21-1P 733776-22-2P
733776-23-3P 733776-24-4P 733776-25-5P 733776-26-6P 733776-27-7P
733776-28-8P 733776-29-9P 733776-30-2P 733776-31-3P 733776-32-4P
733776-33-5P 733776-34-6P 733776-35-7P 733776-36-8P 733776-37-9P
733776-38-0P 733776-39-1P 733776-40-4P 733776-41-5P 733776-43-7P
733776-44-8P 733776-46-0P 733776-47-1P 733776-48-2P 733776-49-3P
733776-50-6P 733776-52-8P 733776-53-9P 733776-54-0P 733776-55-1P
733776-56-2P 733776-57-3P 733776-58-4P 733776-59-5P 733776-60-8P
733776-61-9P 733776-62-0P 733776-63-1P 733776-64-2P 733776-65-3P
733776-66-4P 733776-67-5P 733776-68-6P 733776-69-7P 733776-70-0P
733776-71-1P 733776-72-2P 733776-73-3P 733776-74-4P 733776-75-5P
733776-76-6P 733776-77-7P 733776-78-8P 733776-79-9P 733776-80-2P
733776-81-3P 733776-82-4P 733776-83-5P 733776-84-6P 733776-85-7P
733776-86-8P 733776-87-9P 733776-88-0P 733776-89-1P 733776-90-4P
733776-91-5P 733776-92-6P 733776-93-7P 733776-94-8P 733776-95-9P
733776-96-0P 733776-97-1P 733776-98-2P 733776-99-3P 733777-00-9P
733777-01-0P 733777-02-1P 733777-03-2P 733777-04-3P 733777-05-4P
733777-06-5P 733777-07-6P 733777-08-7P 733777-09-8P 733777-10-1P
733777-11-2P 733777-12-3P 733777-13-4P 733777-14-5P 733777-15-6P
733777-16-7P 733777-17-8P 733777-18-9P 733777-19-0P 733777-20-3P
733777-21-4P 733777-22-5P 733777-23-6P 733777-24-7P 733777-25-8P
733777-26-9P 733777-27-0P 733777-28-1P 733777-29-2P 733777-30-5P
733777-31-6P 733777-32-7P 733777-33-8P 733777-34-9P 733777-35-0P
733777-36-1P 733777-37-2P 733777-38-3P 733777-39-4P 733777-40-7P
733777-41-8P 733777-42-9P 733777-43-0P 733777-44-1P 733777-45-2P
733777-46-3P 733777-47-4P 733777-48-5P 733777-49-6P 733777-50-9P
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733777-56-5P 733777-57-6P 733777-58-7P 733777-59-8P 733777-60-1P
733777-61-2P 733777-62-3P 733777-63-4P 733777-64-5P 733777-65-6P
733777-66-7P 733777-67-8P **733777-68-9P** 733777-69-0P
733777-70-3P 733777-71-4P 733777-72-5P 733777-73-6P 733777-74-7P
733777-75-8P 733777-76-9P 733777-77-0P 733777-78-1P 733777-79-2P
733777-80-5P 733777-81-6P 733777-82-7P 733777-83-8P 733777-84-9P
733777-86-1P 733777-88-3P 733777-90-7P 733777-92-9P 733777-94-1P
733777-96-3P 733777-98-5P 733778-00-2P 733778-02-4P 733778-04-6P
733778-06-8P 733778-07-9P 733778-08-0P 733778-10-4P 733778-12-6P
733778-14-8P 733778-16-0P 733778-18-2P 733778-19-3P 733778-21-7P
733778-22-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 733778-23-9P 733778-24-0P 733778-25-1P 733778-26-2P 733778-27-3P
733778-28-4P 733778-29-5P 733778-30-8P 733778-31-9P 733778-32-0P
733778-33-1P 733778-34-2P 733778-36-4P 733778-37-5P 733778-38-6P
733778-39-7P 733778-40-0P 733778-41-1P 733778-42-2P 733778-43-3P
733778-44-4P 733778-45-5P 733778-46-6P 733778-47-7P 733778-48-8P
733778-49-9P 733778-50-2P 733778-51-3P 733778-52-4P 733778-53-5P
733778-54-6P 733778-55-7P 733778-56-8P 733778-57-9P 733778-58-0P
733778-59-1P 733778-60-4P 733778-61-5P 733778-62-6P 733778-63-7P
733778-64-8P 733778-65-9P 733778-66-0P 733778-67-1P 733778-68-2P
733778-69-3P 733778-70-6P 733778-71-7P 733778-72-8P 733778-73-9P
733778-74-0P 733778-75-1P 733778-76-2P 733778-77-3P 733778-78-4P
733778-79-5P 733778-80-8P 733778-81-9P 733778-82-0P 733778-83-1P
733778-84-2P 733778-85-3P 733778-86-4P 733778-87-5P 733778-88-6P
733778-89-7P 733778-90-0P 733778-94-4P 733778-95-5P 733778-96-6P
733778-97-7P 733778-98-8P 733778-99-9P 733779-00-5P 733779-01-6P
733779-02-7P 733779-03-8P 733779-04-9P 733779-05-0P 733779-06-1P
733779-07-2P 733779-08-3P 733779-09-4P 733779-10-7P 733779-11-8P
733779-12-9P 733779-13-0P 733779-14-1P 733779-15-2P 733779-16-3P
733779-17-4P 733779-18-5P 733779-19-6P 733779-20-9P 733779-21-0P
733779-22-1P 733779-23-2P 733779-24-3P 733779-25-4P 733779-26-5P
733779-27-6P 733779-28-7P 733779-29-8P 733779-30-1P 733779-31-2P
733779-32-3P 733779-33-4P 733779-34-5P 733779-35-6P 733779-36-7P
733779-37-8P 733779-38-9P 733779-39-0P 733779-40-3P 733779-41-4P
733779-42-5P 733779-43-6P 733779-44-7P 733779-45-8P 733779-46-9P
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733779-57-2P 733779-58-3P 733779-59-4P 733779-60-7P 733779-61-8P
733779-62-9P 733779-63-0P 733779-64-1P 733779-65-2P 733779-66-3P
733779-67-4P 733779-68-5P 733779-69-6P 733779-70-9P 733779-71-0P
733779-72-1P 733779-73-2P 733779-74-3P 733779-75-4P 733779-76-5P
733779-77-6P 733779-78-7P 733779-79-8P 733779-80-1P 733779-81-2P
733779-82-3P 733779-83-4P 733779-84-5P 733779-85-6P 733779-86-7P
733779-87-8P 733779-88-9P 733779-89-0P 733779-90-3P 733779-91-4P
733779-92-5P 733779-93-6P 733779-94-7P 733779-95-8P 733779-96-9P
733779-97-0P 733779-98-1P 733779-99-2P 733780-00-2P 733780-01-3P
733780-02-4P 733780-03-5P 733780-04-6P 733780-05-7P 733780-06-8P
733780-07-9P 733780-08-0P 733780-09-1P 733780-10-4P 733780-11-5P
733780-12-6P 733780-13-7P 733780-14-8P 733780-15-9P 733780-16-0P
733780-17-1P 733780-18-2P 733780-19-3P 733780-20-6P 733780-21-7P
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733780-27-3P 733780-28-4P 733780-29-5P 733780-30-8P 733780-31-9P
733780-32-0P 733780-33-1P 733780-34-2P 733780-35-3P 733780-36-4P
733780-37-5P 733780-38-6P 733780-39-7P 733780-40-0P 733780-41-1P
733780-42-2P 733780-43-3P 733780-44-4P 733780-45-5P 733780-46-6P
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733780-52-4P 733780-53-5P 733780-54-6P 733780-55-7P 733780-56-8P
733780-57-9P 733780-58-0P 733780-59-1P 733780-60-4P 733780-61-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 733780-62-6P 733780-63-7P 733780-64-8P 733780-65-9P 733780-66-0P
733780-67-1P 733780-68-2P 733780-69-3P 733780-70-6P 733780-71-7P
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733780-77-3P 733780-78-4P 733780-79-5P 733780-80-8P 733780-81-9P
733780-82-0P 733780-83-1P 733780-84-2P 733780-85-3P 733780-86-4P
733780-87-5P 733780-88-6P 733780-89-7P 733780-90-0P 733780-91-1P
733780-92-2P 733780-93-3P 733780-94-4P 733780-95-5P 733780-96-6P
733780-97-7P 733780-98-8P 733780-99-9P 733781-00-5P 733781-01-6P

733781-02-7P 733781-03-8P 733781-04-9P 733781-05-0P 733781-06-1P
733781-07-2P 733781-08-3P 733781-09-4P 733781-10-7P 733781-11-8P
733781-12-9P 733781-13-0P 733781-14-1P 733781-15-2P 733781-16-3P
733781-17-4P 733781-18-5P 733781-19-6P 733781-20-9P 733781-21-0P
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733781-72-1P 733781-73-2P 733781-74-3P 733781-75-4P 733781-76-5P
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733781-82-3P 733781-83-4P 733781-84-5P 733781-85-6P 733781-86-7P
733781-87-8P 733781-88-9P 733781-89-0P 733781-90-3P 733781-91-4P
733781-92-5P 733781-93-6P 733781-94-7P 733781-95-8P 733781-96-9P
733781-97-0P 733781-98-1P 733781-99-2P 733782-00-8P 733782-01-9P
733782-02-0P 733782-05-3P 733782-07-5P 733782-08-6P 733782-09-7P
733782-10-0P 733782-11-1P 733782-12-2P 733782-13-3P 733782-14-4P
733782-15-5P 733782-16-6P 733782-17-7P 733782-18-8P 733782-19-9P
733782-20-2P 733782-21-3P 733782-22-4P 733782-23-5P 733782-24-6P
733782-25-7P 733782-26-8P 733782-27-9P 733782-28-0P 733782-29-1P
733782-30-4P 733782-31-5P 733782-32-6P 733782-33-7P 733782-34-8P
733782-35-9P 733782-36-0P 733782-37-1P 733782-38-2P 733782-39-3P
733785-81-4P 733785-82-5P 733785-83-6P 733785-84-7P 733785-85-8P
733785-86-9P 733785-87-0P 733785-88-1P 733785-89-2P 733785-90-5P
733785-91-6P 733785-92-7P 733785-93-8P 733785-94-9P 733785-95-0P
733785-96-1P 733785-97-2P 733785-98-3P 733785-99-4P 733786-00-0P
733786-01-1P 733786-02-2P 733786-03-3P 733786-04-4P 733786-05-5P
733786-06-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 75-30-9, 2-Iodopropane 78-84-2 79-03-8, Propionyl chloride 94-09-7, Ethyl p-aminobenzoate 96-22-0, Diethyl ketone 99-76-3, Methyl 4-hydroxybenzoate 99-96-7, 4-Hydroxybenzoic acid, reactions 100-10-7, 4-(Dimethylamino)benzaldehyde 100-36-7, N,N-Diethylethylenediamine 107-30-2, Chloromethyl methyl ether 108-01-0, N,N-Dimethylethanolamine 109-55-7, 3-Dimethylaminopropylamine 109-77-3, Malononitrile 111-36-4, n-Butyl isocyanate 111-44-4, Bis(2-chloroethyl) ether 120-47-8, Ethyl 4-hydroxybenzoate 121-33-5, Vanillin 122-51-0, Triethyl orthoformate 123-08-0, 4-Hydroxybenzaldehyde 123-38-6, Propionaldehyde, reactions 123-75-1, Pyrrolidine, reactions 142-25-6, N,N,N'-Trimethylethylenediamine 349-88-2, 4-Fluorobenzenesulfonyl chloride 372-31-6, Ethyl 4,4,4-trifluoroacetoacetate 451-46-7, Ethyl 4-fluorobenzoate 501-30-4, 5-Hydroxy-2-(hydroxymethyl)-4H-pyranone 513-86-0, Acetoin 527-69-5, 2-Furoyl chloride 541-41-3, Ethyl chloroformate 619-82-9, trans-Cyclohexane-1,4-dicarboxylic acid 628-12-6, 2-Methoxyethyl chloroformate 628-21-7, 1,4-Diiodobutane 628-77-3, 1,5-Diiodopentane 814-68-6, Acryloyl chloride 867-13-0, Triethyl phosphonoacetate 869-24-9 872-85-5, Pyridine-4-carboxaldehyde 1003-03-8, Cyclopentylamine 1074-36-8, 4-Mercaptobenzoic acid 1126-09-6, Ethyl isonipecotate 1197-18-8, trans-4-(Aminomethyl)cyclohexanecarboxylic acid 1571-08-0, Methyl 4-formylbenzoate 1694-92-4, 2-Nitrobenzenesulfonyl chloride 2304-94-1, N-Benzyloxycarbonyl-β-alanine 2417-72-3, Methyl 4-(bromomethyl)benzoate 2605-67-6 2840-26-8, 3-Amino-4-methoxybenzoic acid 3179-63-3, 3-(Dimethylamino)propanol 3647-69-6,

4-(2-Chloroethyl)morpholine hydrochloride 3943-89-3, Ethyl 3,4-dihydroxybenzoate 4023-34-1, Cyclopropylcarbonyl chloride 4530-20-5, N-(tert-Butoxycarbonyl)glycine 4543-96-8, N,N,N'-Trimethylpropane-1,3-diamine 4584-46-7, 2-(Dimethylamino)ethyl chloride hydrochloride 4755-77-5, Ethyl chlorooxoacetate 4897-50-1, 4-Piperidinopiperidine 5004-07-9, 4-(1-Pyrrolidinyl)piperidine 5292-43-3, tert-Butyl bromoacetate 5407-04-5, 3-Chloropropyldimethylamine hydrochloride 5470-70-2, Methyl 6-methylnicotinate 5717-37-3, (1-Ethoxycarbonylethylidene)triphenylphosphorane 6914-74-5, 1-Carbamoyl-1-cyclopropanecarboxylic acid 7151-68-0, 3-Methoxy-4-methylbenzoic acid 7154-73-6, 1-(2-Aminoethyl)pyrrolidine 7377-26-6, Terephthalic acid monomethyl ester chloride 7379-35-3, 4-Chloropyridine hydrochloride 7400-08-0, 4-Hydroxycinnamic acid 13061-96-6, Methylboronic acid 13242-44-9, 2-(Dimethylamino)ethanethiol hydrochloride 13750-81-7, 1-Methyl-2-imidazolecarboxaldehyde 17159-79-4, Ethyl 4-cyclohexanonecarboxylate 18469-52-8, Methyl 4-(aminomethyl)benzoate 19059-68-8, 3-Dimethylamino-2,2-dimethyl-1-propanol 22600-30-2, Methyl 5-aminofuran-2-carboxylate 27372-38-9, 6-Oxo-1,4,5,6-tetrahydropyridazine-3-carboxylic acid 32047-53-3, 1-Amino-2-methyl-2-propanethiol hydrochloride 32529-79-6, Cyclohexane-1,4-dicarboxylic acid monomethyl ester 40357-96-8, 2-Nitrothiophene-4-carboxylic acid 41979-39-9, 4-Piperidone hydrochloride 51359-78-5, 4-(Bromomethyl)benzaldehyde 54401-85-3, Ethyl (4-pyridyl)acetate 54771-24-3, Chlorobutyryl chloride 58656-98-7, tert-Butyl 4-fluorobenzoate 61266-36-2, Methyl 4-(3-hydroxy-1-propynyl)benzoate 61439-53-0, Ethyl 4-benzylaminobenzoate 62327-21-3, tert-Butyl dimethylphosphonoacetate 62456-15-9, Methyl trans-4-aminocyclohexanecarboxylate 73781-91-6, Methyl 6-chloronicotinate 75680-92-1, Ethyl 6-chloropyridazine-3-carboxylate 79463-77-7 104678-18-4, N-Isopropyl-N-(2-methoxyethyl)amine 123876-47-1, Methyl 4-(3-(tosyloxy)propyl)benzoate 125534-03-4, 4-[[2-(Dimethylamino)ethyl]amino]benzaldehyde 156910-49-5, 5-(Ethoxycarbonyl)thiophene-2-carboxylic acid 171050-00-3, tert-Butyl 4-fluoro-3-methylbenzoate 470442-61-6 733785-80-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 714-27-2P 3399-22-2P, Dimethyl trans-cyclohexane-1,4-dicarboxylate 3943-97-3P, Methyl 4-hydroxycinnamate 5117-88-4P, 2-Amino-4,5-dimethyl-3-furonitrile 6302-65-4P, Methyl 4-mercaptobenzoate 10541-82-9P, Ethyl 4-(methylamino)benzoate 15177-67-0P, Mono-methyl trans-cyclohexane-1,4-dicarboxylate 15182-92-0P, 4-[2-(Dimethylamino)ethoxy]benzaldehyde 17334-08-6P, (1-Methyl-1H-imidazole-2-yl)methanol 17847-26-6P 18153-53-2P 18153-54-3P 18153-55-4P, Methyl 4-[3-(dimethylamino)propyl]benzoate 24489-96-1P, Ethyl 3-(4-pyridyl)acrylate 24637-30-7P 25773-00-6P 27237-49-6P, 4-[2-(Dimethylamino)ethoxy]benzoic acid hydrochloride 27687-14-5P, trans-4-(tert-Butoxycarbonylaminomethyl)cyclohexanecarboxylic acid 29275-88-5P, Methyl trans-4-(aminomethyl)cyclohexanecarboxylate hydrochloride 29655-68-3P, Methyl 3-(methylsulfonylamino)-4-methoxybenzoate 37972-69-3P, 6-Oxo-1,6-dihydropyridazine-3-carboxylic acid 38605-39-9P, trans-4-(Dimethylamino)cyclohexanecarboxylic acid 46995-89-5P, 3-Methoxy-4-(2-morpholinoethoxy)benzaldehyde 52902-62-2P, Methyl trans-4-(N-acetylaminomethyl)cyclohexanecarboxylate 53292-89-0P 54274-80-5P, Methyl trans-4-formylcyclohexanecarboxylate 61367-07-5P, Methyl trans-4-aminocyclohexanecarboxylate hydrochloride 64261-07-0P, Ethyl 4-[4-(dimethylamino)benzylamino]benzoate 67318-06-3P 67686-05-9P 68453-37-2P 68453-55-4P 70785-70-5P, Methyl 4-[(methylamino)methyl]benzoate 73278-90-7P 83237-28-9P 84358-13-4P 86649-59-4P 87808-23-9P, Methyl 4-(3-hydroxy-1-propenyl)benzoate 89407-98-7P 89704-62-1P 89999-70-2P 100385-00-0P 105836-43-9P 110928-44-4P, Methyl trans-4-(hydroxymethyl)cyclohexanecarboxylate 117704-80-0P 120157-96-2P, Methyl 4-[[N-(tert-

butoxycarbonyl)amino]methyl]benzoate 124438-69-3P 125104-82-7P 128982-43-4P 131803-48-0P, Methyl 6-(bromomethyl)nicotinate 132521-81-4P 140382-79-2P, Methyl 4-[[N-methyl-N-(tert-butoxycarbonyl)amino]methyl]benzoate 140382-88-3P, trans-4-(N,N-Dimethylaminomethyl)cyclohexanecarboxylic acid hydrochloride 146307-51-9P, Methyl trans-4-(tert-butoxycarbonylamino)cyclohexanecarboxylate 149442-04-6P 153248-46-5P, 1-Hydroxymethyl-1-(tert-butoxycarbonylaminomethyl)cyclopropane 154348-17-1P 154775-43-6P 154934-97-1P, Ethyl 2-hydroxy-4-trifluoromethyl-5-pyrimidinecarboxylate 157688-46-5P 158560-89-5P 160598-45-8P 165947-29-5P 168077-30-3P, Ethyl [1-(4-pyridyl)piperidin-4-yl]acetate 168077-31-4P, [1-(4-Pyridyl)piperidin-4-yl]acetic acid hydrochloride 169458-04-2P, Ethyl 2-(4-piperidyl)acetate hydrochloride 179981-81-8P, Methyl 3-amino-4-methoxybenzoate hydrochloride 187035-79-6P, Ethyl 2-chloro-4-trifluoromethyl-5-pyrimidinecarboxylate 193537-79-0P 193537-82-5P, 1-Propylpiperidin-4-carboxylic acid hydrochloride 193964-24-8P 193964-66-8P 193965-74-1P, Methyl 3-methoxy-4-[(dimethylamino)methyl]benzoate 193966-34-6P 193966-65-3P 215386-65-5P 217810-13-4P 220914-34-1P 262425-15-0P 280774-03-0P, (1-Isopropylpiperidin-4-yl)methanol 280774-04-1P, 1-Isopropylpiperidin-4-carboxaldehyde 314268-40-1P 318280-65-8P 321198-22-5P 343943-37-3P 385785-52-4P, Ethyl 5-aminothiophen-3-carboxylate 400750-49-4P 400899-07-2P, Methyl trans-4-[N-methyl-N-(tert-butoxycarbonyl)amino]cyclohexanecarboxylate 415946-11-1P 415947-00-1P 415954-28-8P 415954-78-8P 444565-47-3P 451461-67-9P 455890-94-5P, N,N-Di-(2-chloroethyl)-2-nitrobenzenesulfonamide 459795-81-4P 473693-40-2P 473987-06-3P, Ethyl 3-(4-piperidyl)propionate hydrochloride 477857-61-7P, Methyl 5-[(cyclopropylcarbonyl)amino]furan-2-carboxylate 609805-41-6P, trans-4-[N-Methyl-N-(tert-butoxycarbonyl)amino]cyclohexanecarboxylic acid 609805-43-8P, Methyl trans-4-(dimethylamino)cyclohexanecarboxylate 609805-44-9P, trans-4-(1-Pyrrolidinyl)cyclohexanecarboxylic acid hydrochloride 609805-45-0P, Methyl trans-4-(1-pyrrolidinyl)cyclohexanecarboxylate 609805-46-1P, trans-4-(Morpholino)cyclohexanecarboxylic acid hydrochloride 609805-47-2P, Methyl trans-4-(morpholino)cyclohexanecarboxylate 609805-51-8P, Methyl trans-4-(N,N-dimethylaminomethyl)cyclohexanecarboxylate 609805-52-9P, Ethyl 3-(1-isopropylpiperidin-4-yl)propionate 609805-53-0P 609805-54-1P, 3-(1-Isopropylpiperidin-4-yl)propionic acid hydrochloride 609805-55-2P 609805-59-6P, 3-(1-Isopropylpiperidin-4-yl)acrylic acid hydrochloride 609805-60-9P, Ethyl 3-(1-isopropylpiperidin-4-yl)acrylate 609805-76-7P, trans-4-(N-Methyl-N-acetylaminomethyl)cyclohexanecarboxylic acid 609805-77-8P, Methyl trans-4-(N-methyl-N-acetylaminomethyl)cyclohexanecarboxylate 658689-29-3P 733046-75-8P 733770-10-0P 733782-40-6P 733782-42-8P 733782-43-9P 733782-44-0P 733782-45-1P 733782-47-3P 733782-49-5P 733782-50-8P 733782-51-9P 733782-52-0P 733782-53-1P 733782-54-2P 733782-55-3P 733782-56-4P 733782-57-5P 733782-58-6P 733782-59-7P 733782-60-0P 733782-61-1P 733782-62-2P 733782-63-3P 733782-64-4P 733782-65-5P 733782-66-6P 733782-67-7P 733782-68-8P 733782-69-9P 733782-70-2P 733782-71-3P, Ethyl 4-[[2-(dimethylamino)ethyl]amino]benzoate 733782-72-4P, Ethyl 4-[N-acryloyl-N-[2-(dimethylamino)ethyl]amino]benzoate 733782-73-5P 733782-74-6P 733782-75-7P 733782-76-8P 733782-77-9P 733782-78-0P 733782-79-1P 733782-80-4P 733782-81-5P 733782-82-6P 733782-83-7P 733782-84-8P 733782-85-9P 733782-86-0P 733782-87-1P 733782-88-2P 733782-89-3P 733782-90-6P 733782-91-7P 733782-92-8P 733782-93-9P 733782-94-0P 733782-95-1P 733782-96-2P 733782-97-3P 733782-98-4P 733782-99-5P 733783-00-1P 733783-01-2P 733783-02-3P 733783-03-4P 733783-04-5P 733783-05-6P 733783-06-7P 733783-07-8P 733783-08-9P 733783-09-0P 733783-10-3P 733783-11-4P 733783-12-5P 733783-13-6P 733783-14-7P 733783-15-8P 733783-16-9P 733783-17-0P 733783-18-1P 733783-19-2P 733783-20-5P 733783-21-6P 733783-22-7P 733783-23-8P 733783-24-9P 733783-25-0P 733783-26-1P 733783-27-2P 733783-28-3P 733783-29-4P 733783-30-7P 733783-31-8P 733783-32-9P 733783-33-0P

733783-34-1P 733783-35-2P 733783-36-3P 733783-37-4P 733783-38-5P, Methyl 4-[[N-ethyl-N-(tert-butoxycarbonyl)amino]methyl]benzoate 733783-39-6P 733783-40-9P, Methyl 3-[N-[2-(diethylamino)ethyl]-N-(methylsulfonyl)amino]-4-methoxybenzoate hydrochloride 733783-41-0P 733783-42-1P 733783-43-2P, Ethyl 1-propylpiperidin-4-carboxylate hydrochloride 733783-44-3P, 4-[N-[(2-Methoxyethoxy)carbonyl]-N-[2-(dimethylamino)ethyl]amino]benzaldehyde 733783-45-4P, Methyl 4-[[[2-(dimethylamino)ethyl]amino]carbonyl]benzoate 733783-46-5P, 2-(1-Isopropylpiperidin-4-yl)ethanol 733783-47-6P, Methyl 4-[[N-methyl-N-[[2-(diethylamino)ethoxy]carbonyl]amino]methyl]benzoate 733783-48-7P, Methyl 5-[N-(cyclopropylcarbonyl)-N-[2-(dimethylamino)ethyl]amino]furan-2-carboxylate 733783-49-8P, Ethyl 5-[(tert-butoxycarbonyl)amino]thiophen-3-carboxylate 733783-50-1P, Ethyl 5-[N-(tert-butoxycarbonyl)-N-[2-(dimethylamino)ethyl]amino]thiophen-3-carboxylate 733783-51-2P, Ethyl 5-[[2-(dimethylamino)ethyl]amino]thiophe n-3-carboxylate 733783-52-3P, Ethyl 5-[N-acetyl-N-[2-(dimethylamino)ethyl]amino]thiophen-3-carboxylate 733783-53-4P, Ethyl 5-[N-(butylcarbamoyl)-N-[2-(dimethylamino)ethyl]amino]thiophen-3-carboxylate 733783-54-5P, Ethyl 5-[[[2-(dimethylamino)ethyl]amino]carbon yl]thiophen-2-carboxylate 733783-55-6P, tert-Butyl 4-[[2-(1-pyrrolidinyl)ethyl]amino]benzoate 733783-56-7P, tert-Butyl 4-[N-acetyl-N-[2-(1-pyrrolidinyl)ethyl]amino]benzoate 733783-57-8P, 3-Methoxy-4-[(dimethylamino)methyl]benzoate hydrochloride 733783-58-9P, Methyl 3-methyl-4-[(dimethylamino)methyl]benzoate 733783-59-0P, Methyl trans-4-[N-(tert-butoxycarbonyl)-N-[2-(dimethylamino)ethyl]amino]cyclohexa necarboxylate 733783-60-3P 733783-61-4P 733783-62-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

IT 733783-63-6P 733783-64-7P 733783-65-8P 733783-66-9P 733783-67-0P 733783-68-1P 733783-69-2P 733783-70-5P 733783-71-6P 733783-72-7P 733783-73-8P 733783-74-9P 733783-75-0P 733783-76-1P 733783-77-2P 733783-78-3P 733783-79-4P 733783-80-7P 733783-81-8P 733783-82-9P 733783-83-0P 733783-84-1P 733783-85-2P 733783-86-3P 733783-87-4P 733783-88-5P 733783-89-6P 733783-90-9P 733783-91-0P 733783-92-1P 733783-93-2P 733783-94-3P 733783-95-4P 733783-96-5P 733783-97-6P 733783-98-7P 733783-99-8P 733784-00-4P 733784-01-5P 733784-02-6P 733784-03-7P 733784-04-8P 733784-05-9P 733784-06-0P 733784-07-1P 733784-08-2P 733784-09-3P 733784-10-6P 733784-11-7P 733784-12-8P 733784-13-9P 733784-14-0P 733784-15-1P 733784-16-2P 733784-17-3P 733784-18-4P 733784-19-5P 733784-20-8P 733784-21-9P 733784-22-0P 733784-23-1P 733784-24-2P 733784-25-3P 733784-26-4P 733784-27-5P 733784-28-6P 733784-29-7P 733784-30-0P 733784-31-1P 733784-32-2P 733784-33-3P 733784-34-4P 733784-35-5P 733784-36-6P 733784-37-7P 733784-38-8P 733784-39-9P 733784-40-2P 733784-41-3P 733784-42-4P 733784-43-5P 733784-44-6P, Methyl 4-[[1-(tert-butoxycarbonylaminomethyl)cyclopropyl]methoxy]benzoate 733784-45-7P, 4-[2-(Dimethylamino)ethylthio]benzoic acid 733784-46-8P, Ethyl trans-4-(methoxymethoxy)cyclohexanecarboxylate 733784-47-9P 733784-48-0P, Ethyl 4-[N-benzyl-N-(4-chlorobutyryl)amino]benzoate 733784-49-1P 733784-50-4P, Ethyl 4-[2-(dimethylamino)ethoxy]-3-hydroxybenzoate 733784-51-5P, Ethyl 3-[4-(bromomethyl)phenyl]-2-methylacrylate 733784-53-7P 733784-54-8P 733784-55-9P, Methyl 4-(N-cyclopentylaminomethyl)benzoate 733784-56-0P, Methyl 4-(N-cyclopentyl-N-methylaminomethyl)benzoate 733784-57-1P, tert-Butyl 4-[[3-(dimethylamino)-2,2-dimethylpropyl]amino]benzoate 733784-58-2P, tert-Butyl 4-[[3-(dimethylamino)-2,2-dimethylpropyl]-N-ethylamino]benzoate 733784-59-3P, Methyl trans-4-[N-(tert-butoxycarbonyl)-N-ethylamino]cyclohexanecarboxylate 733784-60-6P, Ethyl 5,6-dimethyl-4-oxo-3,4-dihydrofuro[2,3-d]pyrimidine-2-carboxylate 733784-62-8P 733784-63-9P, 4-[2-(Dimethylamino)ethoxy]-5,6-dimethylfuro[2,3-d]pyrimidine-2-carboxylic acid 733784-64-0P, tert-Butyl

2-[[6-(hydroxymethyl)-4-oxo-4H-pyran-3-yl]oxy]acetate 733784-65-1P, tert-Butyl 2-[[6-formyl-4-oxo-4H-pyran-3-yl]oxy]acetate 733784-66-2P, tert-Butyl 2-[[4-oxo-6-[(1-pyrrolidinyl)methyl]-4H-pyran-3-yl]oxy]acetate 733784-67-3P, 2-[[4-Oxo-6-[(1-pyrrolidinyl)methyl]-4H-pyran-3-yl]oxy]acetic acid 733784-68-4P 733784-69-5P 733784-70-8P 733784-71-9P, tert-Butyl 4-[[2-(dimethylamino)ethyl]amino]-3-methylbenzoate 733784-72-0P, 4-[[2-(Dimethylamino)ethyl]amino]-3-methylbenzoic acid dihydrochloride 733784-73-1P, Ethyl 2-[N-methyl-N-[2-(dimethylamino)ethyl]amino]-4-trifluoromethyl-5-pyrimidinecarboxylate 733784-74-2P, Methyl trans-4-(dipropylamino)cyclohexanecarboxylate 733784-75-3P, Methyl 4-[3-(dimethylamino)-1-propenyl]benzoate 733784-76-4P, Methyl 4-[3-(1-pyrrolidinyl)-1-propynyl]benzoate 733784-77-5P, 4-[[2-(Dimethylamino)ethyl]amino]benzoic acid dihydrochloride
733784-78-6P 733784-79-7P 733784-80-0P 733784-81-1P 733784-82-2P
733784-83-3P 733784-84-4P 733784-85-5P 733784-86-6P 733784-87-7P
733784-88-8P 733784-89-9P 733784-90-2P 733784-91-3P 733784-92-4P
733784-93-5P 733784-94-6P 733784-95-7P 733784-96-8P 733784-97-9P
733784-98-0P 733784-99-1P 733785-00-7P 733785-01-8P 733785-02-9P
733785-03-0P 733785-04-1P 733785-05-2P 733785-06-3P 733785-07-4P
733785-08-5P 733785-09-6P 733785-10-9P 733785-11-0P 733785-12-1P
733785-13-2P 733785-14-3P 733785-15-4P 733785-16-5P 733785-17-6P
733785-18-7P 733785-19-8P 733785-20-1P 733785-21-2P 733785-22-3P,
Ethyl 6-chloro-1,6-dihydropyridazine-3-carboxylate 733785-23-4P, Ethyl 4-(2-(dimethylamino)ethylamino)cyclohexanecarboxylate 733785-24-5P, Ethyl 4-(3-(dimethylamino)-2,2-dimethylpropoxy)-3-hydroxybenzoate 733785-25-6P, Ethyl 4-(3-(dimethylamino)-2,2-dimethylpropoxy)-3-(2-(morpholin-4-yl)ethoxy)benzoate 733785-26-7P 733785-27-8P, tert-Butyl 4-[(2-amino-1,1-dimethylethyl)thio]benzoate 733785-28-9P, tert-Butyl 4-[(2-(dimethylamino)-1,1-dimethylethyl)thio]benzoate 733785-29-0P, Methyl 4-[(3-(dimethylamino)-2,2-dimethylpropyl)thio]benzoate
733785-30-3P 733785-31-4P 733785-32-5P, Methyl 4-[3-(methylamino)-1-propynyl]benzoate 733785-33-6P 733785-34-7P 733785-35-8P
733785-36-9P 733785-37-0P 733785-38-1P 733785-39-2P 733785-40-5P
733785-41-6P 733785-42-7P 733785-43-8P 733785-44-9P 733785-45-0P
733785-46-1P 733785-47-2P 733785-48-3P 733785-49-4P 733785-50-7P
733785-51-8P 733785-52-9P 733785-53-0P 733785-54-1P 733785-55-2P
733785-56-3P 733785-57-4P 733785-58-5P 733785-59-6P 733785-60-9P
733785-61-0P 733785-62-1P 733785-63-2P 733785-64-3P 733785-65-4P
733785-66-5P 733785-67-6P 733785-68-7P 733785-69-8P 733785-70-1P
733785-71-2P 733785-72-3P 733785-73-4P 733785-74-5P 733785-75-6P
733785-76-7P 733785-78-9P 733785-79-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrazolopyrimidines as a small conductance potassium channel (SK channel) blocking agents)

L7 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:308358 CAPLUS
DN 140:315066
ED Entered STN: 15 Apr 2004
TI Methods and reagents using selective serotonin reuptake inhibitors (SSRIs) and corticosteroids for the treatment of diseases and disorders associated with increased levels of proinflammatory cytokines
IN Manivasakam, Palaniyandi; Smith, Brendan; Fong, Jason; Auspitz, Benjamin A.; Nichols, M. James; Keith, Curtis; Zimmermann, Grant R.; Brasher, Bradley B.; Sachs, Noah; Chappell, Todd W.; Jost-Price, Edward Roydon
PA Combinatorx, Incorporated, USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K

CC 1-7 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004030618	A2	20040415	WO 2003-US30156	20030924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2002-413040P	P	20020924
	US 2002-417261P	P	20021009
	US 2002-427424P	P	20021119
	US 2002-427526P	P	20021119
	US 2003-464753P	P	20030423

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004030618	ICM	A61K

AB The invention discloses a method for treating a patient diagnosed with, or at risk of developing, an immunoinflammatory disorder by administering an SSRI or analog or metabolite thereof and, optionally, a corticosteroid or other compound, to the patient. The invention also features a pharmaceutical composition containing an SSRI or analog or metabolite thereof and a corticosteroid or other compound for the treatment or prevention of an immunoinflammatory disorder.

ST SSRI corticosteroid therapeutic inflammatory cytokine disease; immunoinflammatory disorder therapeutic serotonin reuptake inhibitor corticosteroid

IT Intestine, disease
(Crohn's; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Antirheumatic agents
(DMARD; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(TNF-α; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Spinal column, disease
(ankylosing spondylitis; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Artery, disease
(arteritis, giant cell; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Dermatitis
(atopic; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Health products
(biologicals; selective serotonin reuptake inhibitors and

corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Lung, disease
(chronic obstructive; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Immunity
(disorder; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Drugs
(**gastrointestinal**; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inflammatory; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Anti-inflammatory agents
(nonsteroidal; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Muscle, disease
(polymyalgia rheumatica; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Arthritis
(psoriatic arthritis; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT 5-HT reuptake inhibitors
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Asthma
Bronchodilators
Cardiovascular agents
Cholinergic antagonists
Drug delivery systems
Drug interactions
Drug screening
Human
Immunomodulators
Inflammation
Multiple sclerosis
Myasthenia gravis
Nervous system agents
Psoriasis
Rheumatic diseases
Rheumatoid arthritis
(selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Interleukin 1β
Interleukin 2
Interleukin 4
Interleukin 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Corticosteroids, biological studies
Retinoids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Drug delivery systems
Lupus erythematosus
(systemic; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Drug delivery systems
(topical; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Intestine, disease
(ulcerative colitis; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Adrenoceptor agonists
(β-; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT 329900-75-6, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT 361540-77-4, Calcineurin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nonsteroidal calcineurin inhibitors; selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

IT 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 50-24-8, Prednisolone 51-43-4, Epinephrine 53-03-2, Prednisone 53-06-5, Cortisone 58-55-9, Theophylline, biological studies 59-05-2, Methotrexate 66-97-7D, Psoralen, derivs. 69-89-6D, Xanthine, derivs. 83-43-2, Methylprednisolone 89-57-6, Mesalamine 89-57-6D, 5-Aminosalicylic acid, derivs. 124-94-7, Triamcinolone 298-81-7, Methoxsalen 599-79-1, Sulfasalazine 1406-16-2D, Vitamin D, analogs 2557-49-5, Diflorasone 5874-97-5, Metaproterenol sulfate 6054-98-4, Olsalazine sodium 7683-59-2, Isoproterenol 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 22204-53-1, Naproxen 23031-25-6, Terbutaline 30392-41-7, Bitolterol mesylate 43229-80-7, Formoterol fumarate 50293-90-8, Levalbuterol hydrochloride 51333-22-3, Budesonide 52795-02-5, Tametraline 54739-18-3, Fluvoxamine 54739-19-4, Clovoxamine 54910-89-3, Fluoxetine 55079-83-9, Acitretin 56775-88-3, Zimeldine 59729-33-8, Citalopram 59859-58-4, Femoxetine 59865-13-3, Cyclosporine A 59969-41-4, Ibuterol sulfate 60205-81-4, Ipratropium 60929-23-9, Indeloxazine 61869-08-7, Paroxetine 63758-79-2, Indalpine 65652-44-0, Pirbuterol acetate 66208-11-5, Ifoxetine 72714-74-0, Viqualine 75706-12-6, Leflunomide 79617-96-2, Sertraline **83891-03-6**, Norfluoxetine 86811-09-8, Litoxetine 90566-53-3, Fluticasone 90667-30-4, Cyanodothiepin 92623-85-3, Milnacipran 93413-69-5, Venlafaxine 94749-08-3, Salmeterol xinafoate 100568-02-3, S-Fluoxetine 100568-03-4, R-(+)-Fluoxetine 104987-11-3, Tacrolimus 112922-55-1, Ericlamine 112965-21-6, Calcipotriene 118292-40-3, Tazarotene 119356-77-3, Dapoxetine 128196-01-0, Escitalopram 137071-32-0, Pimecrolimus 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 170277-31-3, Infliximab 181695-72-7, Valdecoxib 185243-69-0, Etanercept 186691-13-4, Tiotropium 213594-60-6,

Balsalazide disodium 220991-20-8, Lumiracoxib 331731-18-1, Adalimumab 368455-04-3, ISAtx247
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective serotonin reuptake inhibitors and corticosteroids for treatment of diseases associated with increased proinflammatory cytokines)

L7 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:141139 CAPLUS
DN 140:296804
ED Entered STN: 20 Feb 2004
TI Stereoselective pharmacokinetics of fluoxetine and norfluoxetine enantiomers in pregnant sheep
AU Kim, John; Riggs, K. Wayne; Rurak, Dan W.
CS BC Research Institute of Children's & Women's Health, Department of Obstetrics and Gynecology, University of British Columbia, Vancouver, BC, Can.
SO Drug Metabolism and Disposition (2004), 32(2), 212-221
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 1-2 (Pharmacology)
AB We examined the stereoselective disposition of fluoxetine (FX) and its metabolite norfluoxetine (NFX) in five pregnant sheep. Racemic FX was administered i.v. to the ewe (50 mg) and the fetus (10 mg) on sep. occasions. Maternal and fetal blood, maternal urine, and fetal amniotic and tracheal fluid samples were collected for 72 h. FX and NFX isomers were quantified by **gas** chromatog.-mass spectrometry. They rapidly crossed the placenta [maternal to fetal area under the plasma concentration vs. time curve (AUC) ratios 0.59 and 0.65, resp.]. There was significant FX stereoselectivity with S/R FX AUC ratios averaging 1.65±0.33 and 1.73±0.29 in ewe and fetus, resp., after maternal dosing. The maternal clearance and volume of distribution were also higher for (R)-fluoxetine than for (S)-fluoxetine. FX, NFX, and their glucuronides were present in maternal urine but accounted for only 3.4% of maternal drug elimination. In contrast, NFX was not detected in the fetus after fetal FX administration, which is consistent with the absence of measurable fetal nonplacental clearance of the drug and the lack of NFX formation in fetal hepatic microsomal incubations. There was also no fetal production of FX and NFX glucuronides in vivo. Both FX and NFX were extensively and stereoselectively bound in maternal and fetal plasma, with the free fraction S/R FX ratio averaging 0.46±0.06 and 0.58±0.10 in ewe and fetus, resp. Thus, FX exhibits extensive stereoselective disposition, which is likely due to differential plasma protein binding of the FX isomers, and there is no detectable fetal formation of NFX, FX, and NFX glucuronides.
ST stereoselective pharmacokinetics fluoxetine norfluoxetine pregnancy
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood, binding; stereoselective pharmacokinetics of fluoxetine and norfluoxetine enantiomers in pregnant sheep)
IT Biological transport
(drug, placental; stereoselective pharmacokinetics of fluoxetine and norfluoxetine enantiomers in pregnant sheep)
IT Pregnancy
(stereoselective pharmacokinetics of fluoxetine and norfluoxetine enantiomers in pregnant sheep)
IT Placenta
(transport; stereoselective pharmacokinetics of fluoxetine and norfluoxetine enantiomers in pregnant sheep)
IT 100568-02-3, (S)-Fluoxetine 100568-03-4, (R)-Fluoxetine
126924-38-7, (S)-Norfluoxetine

RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(stereoselective pharmacokinetics of fluoxetine and norfluoxetine enantiomers in pregnant sheep)

RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Alfaro, C; J Clin Pharmacol 2000, V40, P58 CAPLUS
(2) Anon; Fetal Growth and Development 2001
(3) Bergstrom, R; Br J Psychiatry Suppl 1988, 3, P47 MEDLINE
(4) Cabrera-Vera, T; J Pharmacol Exp Ther 1998, V286, P1474 CAPLUS
(5) Catterson, M; Pharmacol Toxicol 1996, V78, P203 CAPLUS
(6) Chambers, C; N Engl J Med 1996, V335, P1010 CAPLUS
(7) Chambers, C; Pediatrics 1999, V104, Pe61 MEDLINE
(8) Chien, C; AAPS Pharm Sci 1999, V1, PS224
(9) Clark, K; Life Sci 1980, V27, P2655 CAPLUS
(10) Cohen, L; Biol Psychiatry 2000, V48, P996 CAPLUS
(11) Daniel, W; Pharmacol Toxicol 1997, V81, P259 CAPLUS
(12) DeVane, C; Cell Mol Neurobiol 1999, V19, P443 CAPLUS
(13) Di Pasquale, E; Brain Res Dev Brain Res 1994, V80, P222 CAPLUS
(14) Faber, J; Placental Physiology 1983, P79
(15) Fjordside, L; Pharmacogenetics 1999, V9, P55 CAPLUS
(16) Fuller, R; Neuropharmacology 1992, V31, P997 MEDLINE
(17) Galtier, P; Vet Res 1996, V27, P363 CAPLUS
(18) Goldstein, D; J Clin Psychopharmacol 1995, V15, P417 MEDLINE
(19) Gram, L; N Engl J Med 1994, V331, P1354 CAPLUS
(20) Hamelin, B; Clin Pharmacol Ther 1996, V60, P512 CAPLUS
(21) Harding, R; J Dev Physiol (Oxf) 1983, V5, P267 MEDLINE
(22) Hiemke, C; Pharmacol Ther 2000, V85, P11 CAPLUS
(23) Hwang, E; Res Commun Chem Pathol Pharmacol 1980, V29, P79 CAPLUS
(24) Kim, J; AAPS Pharm Sci 1999, V1, PS96
(25) Kim, J; Pharm Res (NY) 1995, V12, PS22
(26) Kim, J; Pharm Res (NY) 1996, V13, PS494
(27) Krishna, R; J Pharm Pharmacol 2002, V54, P801 CAPLUS
(28) Kulin, N; JAMA (J Am Med Assoc) 1998, V279, P609 CAPLUS
(29) Kumar, S; Drug Metab Dispos 2000, V28, P857 CAPLUS
(30) Kumar, S; J Pharmacol Exp Ther 1997, V282, P617 CAPLUS
(31) Kwan, E; Am J Physiol 1995, V269, PR749 CAPLUS
(32) Lemberger, L; J Clin Psychiatry 1985, V46, P14 CAPLUS
(33) Lu, A; Biochem Biophys Res Commun 1972, V46, P1334 CAPLUS
(34) Mhanna, M; Pediatrics 1997, V100, P158 MEDLINE
(35) Milne, R; Drug Metab Dispos 1993, V21, P1151 CAPLUS
(36) Morrison, J; Pediatr Res 2002, V51, P433 CAPLUS
(37) Newport, D; Semin Perinatol 2001, V25, P177 MEDLINE
(38) Nordeng, H; Acta Paediatr 2001, V90, P288 MEDLINE
(39) Nulman, I; N Engl J Med 1997, V336, P258 CAPLUS
(40) Oberlander, T; Pediatr Res 2002, V51, P443 CAPLUS
(41) Olsen, G; J Pharmacol Exp Ther 1988, V247, P576 CAPLUS
(42) Pacifici, G; Clin Pharmacokinet 1992, V23, P449 CAPLUS
(43) Pastuszak, A; JAMA (J Am Med Assoc) 1993, V269, P2246 CAPLUS
(44) Pohland, R; Toxicol Appl Pharmacol 1989, V98, P198 CAPLUS
(45) Riggs, K; J Pharm Sci 1988, V77, P373 CAPLUS
(46) Riggs, K; Pharm Res (NY) 1991, V8, PS284
(47) Ring, J; Pharmacol Ther 1999, V84, P429 CAPLUS
(48) Rurak, D; J Dev Physiol (Oxf) 1991, V15, P33 CAPLUS
(49) Spencer, M; Pediatrics 1993, V92, P721 MEDLINE
(50) Stevens, J; J Pharmacol Exp Ther 1993, V226, P964
(51) Urichuk, L; J Chromatogr Biomed Appl 1997, V698, P103 CAPLUS
(52) von Moltke, L; Psychopharmacology (Berl) 1997, V132, P402 CAPLUS
(53) Vorhees, C; Fundam Appl Toxicol 1994, V23, P194 CAPLUS
(54) Wadelius, M; Clin Pharmacol Ther 1997, V62, P400 CAPLUS
(55) Wang, L; J Pharmacol Exp Ther 1985, V235, P302 CAPLUS
(56) Wilkinson, G; Clin Pharmacol Ther 1975, V18, P377 MEDLINE
(57) Wisner, K; Am J Psychiatry 1993, V150, P1541 MEDLINE

(58) Wong, D; Acta Pharm Nord 1990, V2, P171 CAPLUS
(59) Wright, M; J Pharmacol Exp Ther 1991, V258, P897 CAPLUS
(60) Yeleswaram, K; J Pharmacol Exp Ther 1993, V267, P425 CAPLUS
(61) Yoo, S; J Pharm Sci 1986, V75, P685 CAPLUS

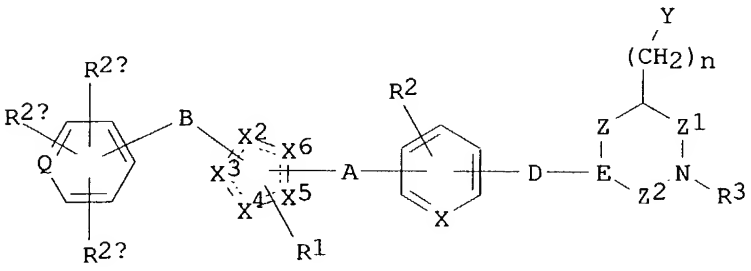
L7 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41231 CAPLUS
DN 140:111429
ED Entered STN: 18 Jan 2004
TI Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents
IN Cheng, Peter T. W.; Chen, Sean; Devasthale, Pratik; Ding, Charles Z.; Herpin, Timothy F.; Wu, Shung; Zhang, Hao; Wang, Wei; Ye, Xiang-Yang
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 543 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004665	A2	20040115	WO 2003-US22149	20030702
	WO 2004004665	A3	20040325		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004063700	A1	20040401	US 2003-616365	20030708
PRAI	US 2002-394508P	P	20020709		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004004665	ICM	A61K

OS MARPAT 140:111429
GI



I

AB The title compds. (I) [Z1 = (CH2)q, CO; Z2 = (CH2)p, CO; D = CH, CO, (CH2)m (where m = 0-3; p = 1, 2; q = 0-2); n = 0-2; Q = C, N; A = (CH2)x (where x = 1-5); A = (CH2)x1 (where x1 = 1-5) with an alkenyl bond or an

alkynyl bond embedded anywhere in the chain; or A = -(CH2)x2-O-(CH2)x3- (where X2, X3 = 0 to 5, provided that at least one of x2 and x3 is other than 0); B = a bond or (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6 = C, N, O, or S and at least one of X2-X6 is C; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halogen, (un)substituted amino; R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, etc.; E = CH, N; Z = (CH2)x5 (where x5 is 0, i.e. a single or a double bond, 1, 2), or Z is (CH2)x6 (where x6 = 2-5), where (CH2)x6 includes an alkenyl (C:C) bond embedded within the chain or Z = -(CH2)x7-O-(CH2)x8- (where x7, x8 = 0-4); (CH2)x to (CH2)x8, (CH2)m, (CH2)n, (CH2)p and (CH2)q may be optionally substituted; Y = CO2R4 (where R4 = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl or aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers, prodrug esters, and pharmaceutically acceptable salts thereof are prepared These compds., e.g. cis-1-ethoxycarbonyl-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidin-3-ylacetic acid and cis-1-(6-trifluoromethylpyrimidin-2-yl)-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidine-3-carboxylic acid, modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) levels, and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia,
hyperlipidemia, obesity, atherosclerosis, and related diseases employing such substituted acid derivs. alone or in combination with another antidiabetic agent and/or a hypolipidemic agent and/ or other therapeutic agents. Disclosed is a method for treating diabetes, especially Type 2 diabetes, and related diseases such as insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, inflammation, Syndrome X, diabetic complications, dysmetabolic syndrome, atherosclerosis, and related diseases, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I. Also disclosed is a method for treating early malignant lesions (such as ductal carcinoma in situ of the breast and lobular carcinoma in situ of the breast), premalignant lesions including fibroadenoma of the breast and prostatic intraepithelial neoplasia (PIN), liposarcomas and various other epithelial tumors (including breast, prostate, colon, ovarian, **gastric** and lung), irritable bowel syndrome, Crohn's disease, **gastric** ulceritis, and osteoporosis and proliferative diseases such as psoriasis, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I.

ST heterocycle prepn antidiabetic antiobesity; oxazolylethoxyphenylpyrrolidineacetic acid prepn antidiabetic antiobesity; oxazolylethoxyphenylpyrimidinylpyrrolidinecarboxylic acid prepn antidiabetic antiobesity; pyrimidinylpyrrolidinecarboxylic acid oxazolylethoxyphenyl prepn antidiabetic antiobesity; pyrrolidineacetic acid oxazolylethoxyphenyl prepn antidiabetic antiobesity; hyperglycemia hyperinsulinemia hyperlipidemia obesity atherosclerosis treatment heterocycle prepn

IT Intestine, disease
(Crohn's; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Intestine, neoplasm
(colon; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Metabolism, animal
(disorder, dysmetabolic syndrome; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Mammary gland, neoplasm
(ductal or lobular carcinoma; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(elevated levels; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Neoplasm
(epithelial; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Stomach, disease
(**gastric** ulceritis; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Intestine, disease
(irritable bowel syndrome; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Adipose tissue, neoplasm
(liposarcoma; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Diabetes mellitus
(non-insulin-dependent; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Anti-inflammatory agents
Antidiabetic agents
Antiobesity agents
Antitumor agents
Antiulcer agents
Atherosclerosis
Cytotoxic agents
Diabetes mellitus
Human
Hyperglycemia
Hypertriglyceridemia
Hypolipemic agents
Inflammation
Lung, neoplasm
Obesity
Osteoporosis
Ovary, neoplasm
Prostate gland, neoplasm
Psoriasis
Stomach, neoplasm
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Heterocyclic compounds
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Disease, animal
(proliferative; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Prostate gland, neoplasm
(prostatic intraepithelial neoplasia; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)
IT Disease, animal
(syndrome X; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan 147511-69-1, Itavastatin 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1, Ezetimibe 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 168273-06-1, Rimonabant 169319-62-4, CGS 30440 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, Balaglitazone 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251565-85-2, AR-H 039242 251572-86-8, P32/98 287714-41-4, Visastatin 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-24-1, ATL-962 335149-25-2, CP331648 416839-88-8, Axokine 430433-17-3, Glipyride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 56-81-5, Glycerol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(elevated levels; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(insulin resistance or hyperinsulinemia; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 647002-99-1P 647003-00-7P 647003-01-8P 647003-02-9P 647003-04-1P 647003-05-2P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 646998-60-9P 646998-64-3P 646998-66-5P 646998-69-8P 646998-72-3P
646998-73-4P 646998-75-6P 646998-77-8P 646998-79-0P 646998-80-3P
646998-83-6P 646998-84-7P 646998-86-9P 646998-88-1P 646998-90-5P
646998-92-7P 646998-93-8P 646998-94-9P 646998-96-1P 646998-98-3P
646999-00-0P 646999-02-2P 646999-04-4P 646999-06-6P 646999-08-8P
646999-10-2P 646999-11-3P 646999-12-4P 646999-13-5P 646999-14-6P
646999-15-7P 646999-16-8P 646999-17-9P 646999-18-0P 646999-19-1P
646999-20-4P 646999-21-5P 646999-22-6P 646999-23-7P 646999-24-8P
646999-25-9P 646999-26-0P 646999-27-1P 646999-28-2P 646999-30-6P
646999-31-7P 646999-32-8P 646999-33-9P 646999-34-0P 646999-35-1P
646999-36-2P 646999-37-3P 646999-38-4P 646999-39-5P 646999-40-8P
646999-41-9P 646999-42-0P 646999-43-1P 646999-44-2P 646999-45-3P

646999-46-4P 646999-47-5P 646999-48-6P 646999-49-7P 646999-50-0P
646999-51-1P 646999-52-2P 646999-53-3P 646999-54-4P 646999-55-5P
646999-56-6P 646999-57-7P 646999-58-8P 646999-59-9P 646999-60-2P
646999-61-3P 646999-62-4P 646999-63-5P 646999-64-6P 646999-65-7P
646999-67-9P 646999-68-0P 646999-69-1P 646999-70-4P 646999-71-5P
646999-72-6P 646999-73-7P 646999-74-8P 646999-75-9P 646999-76-0P
646999-77-1P 646999-78-2P 646999-79-3P 646999-80-6P 646999-81-7P
646999-82-8P 646999-83-9P 646999-84-0P 646999-85-1P 646999-86-2P
646999-87-3P 646999-88-4P 646999-89-5P 646999-90-8P 646999-91-9P
646999-92-0P 646999-93-1P 646999-94-2P 646999-95-3P 646999-96-4P
646999-97-5P 646999-98-6P 646999-99-7P 647000-00-8P 647000-01-9P
647000-02-0P 647000-03-1P 647000-04-2P 647000-05-3P 647000-06-4P
647000-07-5P 647000-08-6P 647000-09-7P 647000-10-0P 647000-11-1P
647000-12-2P 647000-13-3P 647000-14-4P 647000-15-5P 647000-16-6P
647000-17-7P 647000-18-8P 647000-19-9P 647000-20-2P 647000-21-3P
647000-22-4P 647000-23-5P 647000-24-6P 647000-25-7P 647000-26-8P
647000-27-9P 647000-28-0P 647000-29-1P 647000-30-4P 647000-31-5P
647000-32-6P 647000-33-7P 647000-34-8P 647000-35-9P 647000-36-0P
647000-37-1P 647000-38-2P 647000-39-3P 647000-40-6P 647000-41-7P
647000-42-8P 647000-43-9P 647000-44-0P 647000-45-1P 647000-46-2P
647000-47-3P 647000-48-4P 647000-49-5P 647000-50-8P 647000-51-9P
647000-52-0P 647000-53-1P 647000-54-2P 647000-55-3P 647000-56-4P
647000-57-5P 647000-58-6P 647000-59-7P 647000-60-0P 647000-61-1P
647000-62-2P 647000-63-3P 647000-64-4P 647000-65-5P 647000-66-6P
647000-67-7P 647000-68-8P 647000-69-9P 647000-70-2P 647000-71-3P
647000-72-4P 647000-73-5P 647000-74-6P 647000-76-8P 647000-77-9P
647000-78-0P 647000-79-1P 647000-80-4P 647000-81-5P 647000-82-6P
647000-83-7P 647000-84-8P 647000-85-9P 647000-86-0P 647000-87-1P
647000-88-2P 647000-89-3P 647000-90-6P 647000-91-7P 647000-92-8P
647000-93-9P 647000-94-0P 647000-95-1P 647000-96-2P 647000-97-3P
647000-98-4P 647000-99-5P 647001-00-1P 647001-01-2P 647001-02-3P
647001-03-4P 647001-04-5P 647001-05-6P 647001-06-7P 647001-07-8P
647001-08-9P 647001-09-0P 647001-10-3P 647001-11-4P 647001-12-5P
647001-13-6P 647001-14-7P 647001-15-8P 647001-16-9P 647001-17-0P
647001-18-1P 647001-19-2P 647001-20-5P 647001-21-6P 647001-22-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 647001-23-8P 647001-24-9P 647001-25-0P 647001-26-1P 647001-27-2P
647001-28-3P 647001-29-4P 647001-30-7P 647001-31-8P 647001-32-9P
647001-33-0P 647001-34-1P 647001-35-2P 647001-36-3P 647001-37-4P
647001-38-5P 647001-39-6P 647001-40-9P 647001-41-0P 647001-42-1P
647001-43-2P 647001-44-3P 647001-45-4P 647001-46-5P 647001-47-6P
647001-48-7P 647001-49-8P 647001-50-1P 647001-51-2P 647001-52-3P
647001-53-4P 647001-54-5P 647001-55-6P 647001-56-7P 647001-57-8P
647001-58-9P 647001-59-0P 647001-60-3P 647001-61-4P 647001-62-5P
647001-63-6P 647001-64-7P 647001-65-8P 647001-66-9P 647001-67-0P
647001-68-1P 647001-69-2P 647001-70-5P 647001-71-6P 647001-72-7P
647001-73-8P 647001-74-9P 647001-75-0P 647001-76-1P 647001-77-2P
647001-78-3P 647001-79-4P 647001-80-7P 647001-81-8P 647001-82-9P
647001-83-0P 647001-84-1P 647001-85-2P 647001-86-3P 647001-87-4P
647001-88-5P 647001-89-6P 647001-90-9P 647001-91-0P 647001-92-1P
647001-93-2P 647001-94-3P 647001-95-4P 647001-96-5P 647001-97-6P
647001-98-7P 647001-99-8P 647002-00-4P 647002-01-5P 647002-02-6P
647002-03-7P 647002-04-8P 647002-05-9P 647002-06-0P 647002-07-1P
647002-08-2P 647002-09-3P 647002-10-6P 647002-11-7P 647002-12-8P
647002-13-9P 647002-14-0P 647002-15-1P 647002-16-2P 647002-17-3P
647002-18-4P 647002-19-5P 647002-20-8P 647002-21-9P 647002-22-0P
647002-23-1P 647002-24-2P 647002-25-3P 647002-27-5P 647002-28-6P
647002-29-7P 647002-30-0P 647002-31-1P 647002-32-2P 647002-33-3P
647002-34-4P 647002-35-5P 647002-36-6P 647002-37-7P 647002-38-8P

647002-39-9P 647002-40-2P 647002-41-3P 647002-42-4P 647002-43-5P
647002-44-6P 647002-45-7P 647002-46-8P 647002-47-9P 647002-49-1P
647002-50-4P 647002-51-5P 647002-52-6P 647002-53-7P 647002-54-8P
647002-55-9P 647002-56-0P 647002-57-1P 647002-58-2P 647002-59-3P
647002-60-6P 647002-61-7P 647002-62-8P 647002-63-9P 647002-64-0P
647002-65-1P 647002-66-2P 647002-67-3P 647002-68-4P 647002-69-5P
647002-70-8P 647002-71-9P 647002-72-0P 647002-73-1P 647002-74-2P
647002-75-3P 647002-76-4P 647002-77-5P 647002-78-6P 647002-79-7P
647002-80-0P 647002-81-1P 647002-82-2P 647002-83-3P 647002-84-4P
647002-85-5P 647002-86-6P 647002-87-7P 647002-88-8P 647002-89-9P
647002-90-2P 647002-91-3P 647002-92-4P 647002-93-5P 647002-94-6P
647002-95-7P 647002-96-8P 647002-97-9P 647002-98-0P 647003-03-0P
647003-06-3P 647003-07-4P 647003-08-5P 647003-09-6P 647003-10-9P
647003-11-0P 647003-12-1P 647003-13-2P 647003-14-3P 647003-15-4P
647003-16-5P 647003-17-6P 647003-18-7P 647003-19-8P 647003-20-1P
647003-21-2P 647003-22-3P 647003-23-4P 647003-24-5P 647003-25-6P
647003-26-7P 647003-27-8P 647003-28-9P 647003-29-0P 647003-30-3P
647003-31-4P 647003-32-5P 647003-33-6P 647003-34-7P 647003-35-8P
647003-36-9P 647003-37-0P 647003-38-1P 647003-39-2P 647003-40-5P
647003-41-6P 647003-42-7P 647003-43-8P 647003-44-9P 647003-45-0P
647003-46-1P 647003-47-2P 647003-48-3P 647003-49-4P 647003-50-7P
647003-51-8P 647003-52-9P 647003-53-0P 647003-54-1P 647003-55-2P
647003-56-3P 647003-57-4P 647003-58-5P 647003-59-6P 647003-60-9P
647003-61-0P 647003-62-1P 647003-63-2P 647003-64-3P 647003-65-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 647003-66-5P 647003-67-6P 647003-68-7P 647003-69-8P 647003-70-1P
647003-71-2P 647003-72-3P 647003-93-8P 647004-00-0P 647004-07-7P
647004-67-9P 647007-28-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 647004-06-6P 647005-23-0P 647005-27-4P 647005-28-5P 647005-47-8P
647005-49-0P 647005-50-3P 647006-01-7P 647006-03-9P 647006-37-9P
647006-38-0P 647006-51-7P 647006-52-8P 647007-34-9P 647007-35-0P
647007-43-0P 647007-44-1P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 94594-90-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 334-88-3P, Diazomethane 1201-68-9P 3272-96-6P 6129-15-3P
17944-68-2P 24764-91-8P 27492-46-2P 36187-69-6P 39514-19-7P
40019-44-1P 53215-95-5P 57668-34-5P 58608-98-3P 61389-68-2P
85136-12-5P 92427-80-0P 93102-05-7P 94938-02-0P 94938-03-1P
96013-77-3P 96013-95-5P 103788-59-6P 114564-74-8P 116381-09-0P
121484-76-2P 129649-12-3P 131362-25-9P 136058-69-0P 160721-23-3P
161670-81-1P 166253-36-7P 167147-68-4P 175204-39-4P 175204-40-7P
177259-98-2P 185679-37-2P 227029-27-8P 244152-94-1P 255876-57-4P
331746-05-5P 331746-50-0P 433289-57-7P 433289-59-9P 440365-13-9P
476458-89-6P 477541-29-0P 477541-33-6P 477774-06-4P 477774-28-0P
477774-29-1P 477774-36-0P 478540-87-3P 518343-85-6P 585569-20-6P
585569-21-7P 585569-22-8P 585569-23-9P 585569-24-0P 645392-01-4P
645392-34-3P 647003-73-4P 647003-74-5P 647003-75-6P 647003-76-7P
647003-77-8P 647003-78-9P 647003-79-0P 647003-80-3P 647003-81-4P

647003-82-5P 647003-83-6P 647003-84-7P 647003-85-8P 647003-86-9P
647003-87-0P 647003-88-1P 647003-89-2P 647003-90-5P 647003-92-7P
647003-94-9P 647003-95-0P 647003-96-1P 647003-97-2P 647003-98-3P
647003-99-4P 647004-01-1P 647004-02-2P 647004-03-3P 647004-04-4P
647004-05-5P 647004-08-8P 647004-09-9P 647004-10-2P 647004-11-3P
647004-12-4P 647004-13-5P 647004-14-6P 647004-15-7P 647004-16-8P
647004-17-9P 647004-18-0P 647004-19-1P 647004-20-4P 647004-21-5P
647004-22-6P 647004-23-7P 647004-24-8P 647004-25-9P 647004-26-0P
647004-28-2P 647004-29-3P 647004-30-6P 647004-31-7P 647004-32-8P
647004-33-9P 647004-34-0P 647004-35-1P 647004-36-2P 647004-37-3P
647004-38-4P 647004-39-5P 647004-40-8P 647004-41-9P 647004-42-0P
647004-43-1P 647004-44-2P 647004-45-3P 647004-46-4P 647004-47-5P
647004-48-6P 647004-49-7P 647004-50-0P 647004-51-1P 647004-53-3P
647004-54-4P 647004-55-5P 647004-56-6P 647004-57-7P 647004-58-8P
647004-59-9P 647004-60-2P 647004-61-3P 647004-62-4P 647004-63-5P
647004-64-6P 647004-65-7P 647004-66-8P 647004-68-0P 647004-69-1P
647004-70-4P 647004-71-5P 647004-72-6P 647004-73-7P
647004-74-8P 647004-75-9P 647004-76-0P 647004-77-1P 647004-78-2P
647004-79-3P 647004-80-6P 647004-81-7P 647004-82-8P 647004-83-9P
647004-84-0P 647004-85-1P 647004-86-2P 647004-87-3P 647004-88-4P
647004-89-5P 647004-90-8P 647004-91-9P 647004-92-0P 647004-93-1P
647004-94-2P 647004-95-3P 647004-96-4P 647004-97-5P 647004-98-6P
647004-99-7P 647005-00-3P 647005-01-4P 647005-02-5P 647005-03-6P
647005-04-7P 647005-05-8P 647005-06-9P 647005-07-0P 647005-08-1P
647005-09-2P 647005-10-5P 647005-11-6P 647005-12-7P 647005-13-8P
647005-14-9P 647005-15-0P 647005-16-1P 647005-17-2P 647005-18-3P
647005-19-4P 647005-20-7P 647005-21-8P 647005-22-9P 647005-24-1P
647005-25-2P 647005-26-3P 647005-29-6P 647005-30-9P 647005-31-0P
647005-32-1P 647005-33-2P 647005-34-3P 647005-35-4P 647005-36-5P
647005-37-6P 647005-38-7P 647005-39-8P 647005-40-1P 647005-41-2P
647005-42-3P 647005-43-4P 647005-44-5P 647005-45-6P 647005-46-7P
647005-48-9P 647005-51-4P 647005-52-5P 647005-53-6P 647005-54-7P
647005-55-8P 647005-56-9P 647005-57-0P 647005-58-1P 647005-59-2P
647005-60-5P 647005-61-6P 647005-62-7P 647005-63-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 647005-64-9P 647005-65-0P 647005-66-1P 647005-67-2P 647005-68-3P
647005-69-4P 647005-70-7P 647005-71-8P 647005-72-9P 647005-73-0P
647005-74-1P 647005-75-2P 647005-76-3P 647005-77-4P
647005-78-5P 647005-79-6P 647005-80-9P 647005-81-0P 647005-82-1P
647005-83-2P 647005-84-3P 647005-85-4P 647005-86-5P 647005-87-6P
647005-88-7P 647005-89-8P 647005-90-1P 647005-91-2P 647005-92-3P
647005-94-5P 647005-95-6P 647005-96-7P 647005-97-8P 647005-98-9P
647005-99-0P 647006-00-6P 647006-02-8P 647006-05-1P 647006-06-2P
647006-07-3P 647006-08-4P 647006-09-5P 647006-10-8P 647006-11-9P
647006-12-0P 647006-13-1P 647006-14-2P 647006-16-4P 647006-17-5P
647006-18-6P 647006-19-7P 647006-20-0P 647006-21-1P 647006-22-2P
647006-23-3P 647006-24-4P 647006-25-5P 647006-26-6P 647006-27-7P
647006-28-8P 647006-29-9P 647006-30-2P 647006-31-3P 647006-32-4P
647006-33-5P 647006-34-6P 647006-35-7P 647006-36-8P 647006-39-1P
647006-40-4P 647006-41-5P 647006-42-6P 647006-43-7P 647006-44-8P
647006-45-9P 647006-46-0P 647006-47-1P 647006-48-2P 647006-49-3P
647006-50-6P 647006-53-9P 647006-54-0P 647006-55-1P 647006-56-2P
647006-57-3P 647006-58-4P 647006-59-5P 647006-60-8P 647006-61-9P
647006-62-0P 647006-63-1P 647006-64-2P 647006-65-3P 647006-66-4P
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647006-77-7P 647006-78-8P 647006-79-9P 647006-80-2P 647006-81-3P
647006-82-4P 647006-83-5P 647006-84-6P 647006-85-7P 647006-86-8P
647006-87-9P 647006-88-0P 647006-89-1P 647006-90-4P 647006-91-5P
647006-92-6P 647006-93-7P 647006-94-8P 647006-95-9P 647006-96-0P

647006-97-1P 647006-98-2P 647006-99-3P 647007-00-9P 647007-01-0P
647007-02-1P 647007-03-2P 647007-04-3P 647007-05-4P 647007-06-5P
647007-07-6P 647007-08-7P 647007-09-8P 647007-10-1P 647007-11-2P
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647007-17-8P 647007-18-9P 647007-19-0P 647007-20-3P 647007-21-4P
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647007-27-0P 647007-29-2P 647007-30-5P 647007-31-6P 647007-32-7P
647007-33-8P 647007-36-1P 647007-37-2P 647007-38-3P 647007-39-4P
647007-40-7P 647007-41-8P 647007-42-9P 647007-45-2P 647007-46-3P
647007-47-4P 647007-48-5P 647007-49-6P 647007-50-9P 647007-51-0P
647007-52-1P 647007-53-2P 647007-54-3P 647007-55-4P 647007-56-5P
647007-57-6P 647007-58-7P 647007-59-8P 647007-60-1P 647007-61-2P
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647007-68-9P 647007-69-0P 647007-70-3P 647007-71-4P 647007-72-5P
647007-73-6P 647007-74-7P 647007-75-8P 647007-77-0P 647007-79-2P
647007-80-5P 647007-81-6P 647007-82-7P 647012-33-7P 647015-46-1P
647832-88-0P 647832-89-1P 647832-90-4P 647832-91-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 50-00-0, Formaldehyde, reactions 57-71-6, 2,3-Butanedione monooxime 67-56-1, Methanol, reactions 70-25-7, 1-Methyl-3-nitro-1-nitrosoguanidine 75-36-5, Acetyl chloride 77-78-1, Dimethyl sulfate 79-04-9 79-22-1, Methyl chloroformate 88-10-8, Diethylaminocarbonyl chloride 98-09-9, Benzenesulfonyl chloride 98-80-6, Phenylboronic acid 98-88-4, Benzoyl chloride 99-76-3, 4-Hydroxybenzoic acid methyl ester 100-07-2, 4-Methoxybenzoyl chloride 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 100-63-0, Phenylhydrazine 100-83-4, 3-Hydroxybenzaldehyde 103-71-9, Phenyl isocyanate, reactions 103-80-0, Benzeneacetyl chloride 104-94-9, p-Anisidine 106-93-4, 1,2-Dibromoethane 107-13-1, Acrylonitrile, reactions 107-14-2, Chloroacetonitrile 107-21-1, Ethylene glycol, reactions 107-22-2, Glyoxal 108-23-6, Isopropyl chloroformate 108-24-7, Acetic anhydride 108-86-1, Bromobenzene, reactions 109-61-5, n-Propyl chloroformate 109-90-0, Ethyl isocyanate 122-01-0, 4-Chlorobenzoyl chloride 123-08-0, 4-Hydroxybenzaldehyde 124-63-0, Methanesulfonyl chloride 141-75-3, Butyryl chloride 149-87-1, DL-Pyroglutamic acid 312-94-7, 2-Trifluoromethylbenzoyl chloride 329-15-7, 4-Trifluoromethylbenzoyl chloride 375-72-4, 1,1,2,2,3,3,4,4,4-Nonafluoro-1-butanesulfonyl fluoride 431-35-6, Bromotrifluoroacetone 462-27-1, 2-Fluoroethyl chloroformate 501-53-1, Benzyl chloroformate 501-97-3, 3-(4-Hydroxyphenyl)propionic acid 540-38-5, 4-Iodophenol 541-41-3, Ethyl chloroformate 543-27-1, Isobutyl chloroformate 592-34-7, n-Butyl chloroformate 594-44-5, Ethanesulfonyl chloride 615-18-9, 2-Chlorobenzoxazole 616-38-6, Dimethyl carbonate 618-46-2, 3-Chlorobenzoyl chloride 620-24-6, 3-Hydroxybenzyl alcohol 621-54-5, 3-(3-Hydroxyphenyl)propionic acid 623-47-2, Ethyl propynoate 627-11-2, 2-Chloroethyl chloroformate 628-12-6, 2-Methoxyethyl chloroformate 630-08-0, Carbon monoxide, reactions 674-82-8, Diketene 874-60-2, 4-Methylbenzoyl chloride 917-54-4, Methyllithium 917-95-3, 2-Nitroso-2-methylpropane 922-67-8, Methyl propynoate 933-88-0, 2-Methylbenzoyl chloride 937-62-2, 4-Methylphenyl chloroformate 1011-37-6, 5-Chloromethyl-3-phenylisoxazole 1066-54-2, Trimethylsilylacetylene 1118-02-1, Trimethylsilyl isocyanate 1423-26-3, 3-Trifluoromethylphenylboronic acid 1679-18-1, 4-Chlorophenylboronic acid 1700-37-4, 3-Benzyloxybenzaldehyde 1710-98-1, 4-tert-Butylbenzoyl chloride 1711-05-3, 3-Methoxybenzoyl chloride 1711-06-4, 3-Methylbenzoyl chloride 1722-12-9, 2-Chloropyrimidine 1765-93-1, 4-Fluorophenylboronic acid 1822-94-2, 5-Chloromethyl-3-phenyl-[1,2,4]oxadiazole 1885-14-9, Phenyl chloroformate 2251-65-2, 3-Trifluoromethylbenzoyl chloride 2293-75-6, 2-Methoxyphenyl chloroformate 2344-80-1, Chloromethyltrimethylsilane

2393-23-9, 4-Methoxybenzylamine 2605-67-6, Methoxycarbonylmethylenetriph
enylphosphorane 2719-27-9, Cyclohexanecarbonyl chloride 2920-38-9,
4-Biphenylcarbonitrile 2937-50-0, Allyl chloroformate 3282-30-2,
Pivaloyl chloride 3483-82-7, N-Benzoyl-L-tyrosine ethyl ester
3934-20-1, 2,4-Dichloropyrimidine 4210-32-6, 4-tert-Butylbenzonitrile
4285-42-1, N-Methyl-N-phenylcarbamoyl chloride 4397-53-9,
4-Benzyloxybenzaldehyde 4457-32-3, 4-Nitrobenzyl chloroformate
4774-14-5, 2,6-Dichloropyrazine 4949-44-4, Ethyl propionylacetate
5424-21-5, 2,4-Dichloro-6-methylpyrimidine 5470-11-1, Hydroxylamine
hydrochloride 7065-46-5, 3,3-Dimethylbutanoyl chloride 7497-61-2,
3-(3-Hydroxyphenyl)propionic acid methyl ester 7693-41-6,
4-Methoxyphenyl chloroformate 7693-44-9, 4-Bromophenyl chloroformate
7693-45-0, 4-Chlorophenyl chloroformate 7693-50-7, 2-Naphthyl
chloroformate 7803-49-8, Hydroxylamine, reactions 10401-11-3,
3-Hydroxyphenylacetylene 10442-39-4, Tetrabutylammonium cyanide
13045-13-1, 3-Chloro-5-hydroxy-2-pentanone 13398-94-2,
2-(3-Hydroxyphenyl)ethanol 13831-03-3, tert-Butyl propiolate
14210-25-4, 5-Chloro-1-phenyltetrazole 14731-10-3 16205-84-8, Ethyl
3-trimethylsilylpropynoate 18107-18-1, Trimethylsilyldiazomethane
18162-48-6, tert-Butyldimethylsilyl chloride 19358-41-9, 2-Chlorophenyl
chloroformate 19438-10-9, 3-Hydroxybenzoic acid methyl ester
20412-38-8, 2,2-Dimethylpropyl chloroformate 21615-34-9,
2-Methoxybenzoyl chloride 23795-02-0 24424-99-5, Di-tert-butyl
dicarbonate 25054-53-9, 3,4-Methylenedioxybenzoyl chloride 26628-22-8,
Sodium azide 31140-40-6, 4-Methoxycarbonylphenyl chloroformate
32779-36-5, 2-Chloro-5-bromopyrimidine 32807-28-6, Methyl
4-chloroacetoacetate 33034-67-2, 2-Chloro-4-trifluoromethylpyrimidine
35000-38-5, tert-Butyl (triphenylphosphoranylidene)acetate 35718-08-2,
Propargyl chloroformate 36637-44-2, 4-(2-Tetrahydropyranyloxy)phenylmagn
esium bromide 36823-88-8, 4-Trifluoromethoxybenzoyl chloride
38377-38-7, 4-Fluorophenyl chloroformate 39545-31-8, 2-Chlorobenzyl
chloroformate 51067-38-0, 4-Phenoxyphenylboronic acid 52763-21-0,
Ethyl 1-benzyl-3-oxo-4-piperidine carboxylate hydrochloride 68282-47-3,
4-Formyl-2-phenylimidazole 86270-03-3, 3-Trifluoromethoxybenzoyl
chloride 87199-18-6, 3-Hydroxyphenylboronic acid 88738-78-7,
Bis(2,2,2-trifluoroethyl) (methoxycarbonylmethyl)phosphonate 95668-29-4,
3-Trifluoromethylphenyl chloroformate 98946-18-0, tert-Butyl
2,2,2-trichloroacetimidate 103788-65-4 107539-52-6,
4-tert-Butyldimethylsilyloxyphenylmagnesium bromide 108448-77-7
111196-81-7, 2-Chloro-5-ethylpyrimidine 123324-71-0,
p-tert-Butylphenylboronic acid 129714-97-2, 3,5-Difluorobenzoyl chloride
163105-89-3, 6-Methoxy-3-pyridylboronic acid 179915-71-0 183742-23-6
189032-84-6, 3-Methoxyphenylmagnesium chloride 211115-05-8 218278-58-1
312693-16-6, 3-Methoxybenzylzinc chloride 312693-17-7 647007-76-9
647007-78-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 13036-57-2P 103788-61-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reactant; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L7 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41224 CAPLUS
DN 140:111417
ED Entered STN: 18 Jan 2004
TI Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents
IN Cheng, Peter T. W.; Chen, Sean; Ding, Charles Z.; Herpin, Timothy F.
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 160 pp.

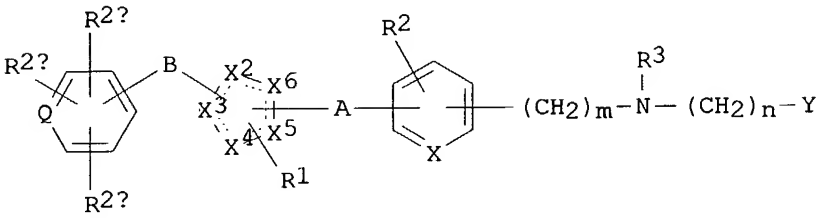
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004655	A2	20040115	WO 2003-US21331	20030708
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004063762	A1	20040401	US 2003-616283	20030708
PRAI	US 2002-394553P	P	20020709		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004004655	ICM	A61K

OS MARPAT 140:111417
GI



I

AB Compds. having general structure (I) [Q = C, N; A = (un)substituted (CH2)x (where x = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain, or A = (un)substituted -(CH2)x2-O-(CH2)x3- (where x2, x3 = 0-5, provided that at least one of x2 and x3 is other than 0); B = a bond, (un)substituted (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6= C, N, O, or S, provided that at least one of X2-X6 is N; and at least one of X2, X3, X4, X5 and X6 is C; R1 = H, alkyl; R2, R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, etc.; Y = CO2R (where R = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl, aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof are prepared These compds. such as N-[[4-(1,2,3-triazol-4-ylmethoxy)benzyl](4-methoxypheoxycarbonyl)amino]acetic acid N-[[4-[2-(1,2,3-triazol-4-yl)ethoxy]benzyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(2- or

4-imidazolylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(1,2,4-oxadiazol-3-ylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[4-(1,2,4-oxadiazol-3-ylmethoxy)phenethyl](isobutoxycarbonyl)amino]acetic acid derivs. modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases.

ST triazole imidazole oxadiazole prepn antiobesity antidiabetic; heterocycle prepn antiobesity antidiabetic; hyperglycemia hyperinsulinemia hyperlipidemia atherosclerosis treatment heterocycle prepn; triazolylmethoxybenzylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; triazolylethoxybenzylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; imidazolylmethoxyphenylisopentylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; oxadiazolylmethoxyphenylisopentylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; oxadiazolylmethoxyphenethylisobutoxycarbonylamino acetic acid prepn antiobesity antidiabetic

IT Intestine, disease
(Crohn's; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Intestine, neoplasm
(colon; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Metabolism, animal
(disorder, dysmetabolic syndrome; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Mammary gland, neoplasm
(ductal carcinoma; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(elevated blood levels; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Neoplasm
(epithelial; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Mammary gland, neoplasm
(fibroadenoma; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Stomach, disease
(**gastric** ulceritis; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Intestine, disease
(irritable bowel syndrome; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Adipose tissue, neoplasm
(liposarcoma; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Carcinoma
(lobular; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Diabetes mellitus
(non-insulin-dependent; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Anti-inflammatory agents
Antidiabetic agents
Antiobesity agents
Antitumor agents
Antiulcer agents
Atherosclerosis
Cytotoxic agents
Diabetes mellitus
Human
Hyperglycemia
Hypertriglyceridemia
Hypolipemic agents
Inflammation
Lung, neoplasm
Neoplasm
Obesity
Osteoporosis
Ovary, neoplasm
Psoriasis
Stomach, neoplasm
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Heterocyclic compounds
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Disease, animal
(proliferative; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Prostate gland, neoplasm
(prostatic intraepithelial neoplasia (PIN); preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT Disease, animal
(syndrome X; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1, Ezetimibe 166518-60-1, Avasimibe 168273-06-1, Rimonabant 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4

199113-98-9, Balaglitazone 199914-96-0, YM-440 213252-19-8, KRP297
244081-42-3, AJ9677 251572-86-8, P32/98 287714-41-4 335149-08-1,
L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, ARHO
39242 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-24-1,
ATL-962 335149-25-2, CP331648 416839-88-8, Axokine 430433-17-3,
Glipyride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 56-81-5, Glycerol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(elevated blood levels; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 645392-65-0P, (R)-(+)-[1-[4-(tert-Butyldimethylsilyloxy)phenyl]ethylamino] acetic acid methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 13322-19-5P 645390-64-3P 645390-65-4P 645390-66-5P 645390-67-6P
645390-68-7P 645390-69-8P 645390-70-1P 645390-71-2P 645390-72-3P
645390-73-4P 645390-74-5P 645390-75-6P 645390-76-7P 645390-77-8P
645390-78-9P 645390-79-0P 645390-80-3P 645390-81-4P 645390-82-5P
645390-83-6P 645390-84-7P 645390-85-8P 645390-86-9P 645390-87-0P
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645391-50-0P 645391-53-3P 645399-36-6P 645399-38-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 100-83-4, 3-Hydroxybenzaldehyde 123-08-0, 4-Hydroxybenzaldehyde
151-50-8, Potassium cyanide 5680-79-5, Glycine methyl ester hydrochloride 7693-41-6, 4-Methoxyphenyl chloroformate 22300-56-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 1201-68-9P 2411-77-0P 3272-96-6P 13322-02-6P 13322-20-8P
17944-68-2P 26787-75-7P 36187-69-6P 94938-02-0P 94938-03-1P
96013-95-5P 99280-78-1P 114564-74-8P 116381-09-0P 143589-99-5P
161670-81-1P 196810-82-9P 255876-57-4P 331746-09-9P 385383-45-9P
440365-13-9P 645391-55-5P 645391-57-7P 645391-59-9P 645391-61-3P
645391-62-4P 645391-63-5P 645391-64-6P 645391-65-7P 645391-66-8P
645391-67-9P 645391-68-0P 645391-69-1P 645391-70-4P 645391-71-5P
645391-72-6P 645391-73-7P 645391-74-8P 645391-75-9P 645391-76-0P
645391-77-1P 645391-78-2P 645391-79-3P 645391-80-6P 645391-81-7P
645391-82-8P 645391-83-9P 645391-84-0P 645391-85-1P 645391-86-2P
645391-87-3P 645391-89-5P 645391-91-9P 645391-93-1P 645391-94-2P
645391-96-4P 645391-99-7P 645392-01-4P 645392-03-6P 645392-05-8P
645392-07-0P **645392-08-1P** 645392-10-5P 645392-12-7P
645392-13-8P 645392-14-9P 645392-15-0P 645392-16-1P 645392-17-2P
645392-18-3P 645392-19-4P 645392-20-7P 645392-21-8P

645392-22-9P 645392-23-0P 645392-24-1P 645392-25-2P
645392-26-3P 645392-27-4P 645392-28-5P 645392-29-6P 645392-30-9P
645392-31-0P 645392-32-1P 645392-33-2P 645392-34-3P 645392-35-4P
645392-36-5P 645392-37-6P 645392-38-7P 645392-40-1P 645392-43-4P
645392-45-6P 645392-47-8P 645392-49-0P 645392-52-5P 645392-54-7P
645392-56-9P 645392-58-1P 645392-61-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 74-88-4, Iodomethane, reactions 75-21-8, Ethylene oxide, reactions 77-78-1, Dimethyl sulfate 79-22-1, Methyl chloroformate 96-32-2, Methyl bromoacetate 98-88-4, Benzoyl chloride 106-93-4, 1,2-Dibromoethane 107-14-2, Chloroacetonitrile 124-63-0, Methanesulfonyl chloride 501-53-1, Benzyl chloroformate 543-27-1, Isobutyl chloroformate 670-95-1, 4-Phenylimidazole 874-60-2, p-Toluoyl chloride 874-90-8, 4-Methoxybenzonitrile 926-62-5, Isobutylmagnesium bromide 1535-73-5, 3-Trifluoromethoxyaniline 1888-75-1, Isopropyllithium 4949-44-4, Ethyl propionylacetate 5470-11-1, Hydroxylamine hydrochloride 7803-49-8, Hydroxylamine, reactions 10442-39-4, Tetrabutylammonium cyanide 18107-18-1, Trimethylsilyldiazomethane 18162-48-6, tert-Butyldimethylsilyl chloride 22038-86-4, (R)-(+)-1-(4-Methoxyphenyl)ethylamine 22818-40-2, D-4-Hydroxyphenylglycine 26628-22-8, Sodium azide 32807-28-6, Methyl 4-chloroacetoacetate 41851-59-6, (S)-1-(4-Methoxyphenyl)ethylamine 68282-47-3, 4-Formyl-2-phenylimidazole 82796-69-8, (S)-1-(3-Methoxyphenyl)ethylamine 157141-27-0, Cyanomethylenetributylphosphorane
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance or hyperinsulinemia; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L7 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:747138 CAPLUS
DN 139:392238
ED Entered STN: 24 Sep 2003
TI Toxicological Screening with Formula-Based Metabolite Identification by Liquid Chromatography/Time-of-Flight Mass Spectrometry
AU Pelander, Anna; Ojanperae, Ilkka; Laks, Suvi; Rasanen, Ilpo; Vuori, Erkki
CS Department of Forensic Medicine, University of Helsinki, FIN-00014, Finland
SO Analytical Chemistry (2003), 75(21), 5710-5718
CODEN: ANCHAM; ISSN: 0003-2700
PB American Chemical Society
DT Journal
LA English
CC 4-2 (Toxicology)
Section cross-reference(s): 1
AB An anal. procedure was evaluated for the comprehensive toxicol. screening of drugs, metabolites, and pesticides in 1-mL urine samples by TurboIon spray liquid chromatog./time-of-flight mass spectrometry (LC/TOFMS) in the pos. ionization mode and continuous mass measurement. The substance database consisted of exact monoisotopic masses for 637 compds., of which an LC retention time was available for 392. A macroprogram was refined for extracting the data into a legible report, utilizing metabolic patterns and preset identification criteria. These criteria included ±30 ppm mass tolerance, a ±0.2-min window for absolute retention time, if available, and a min. area count of 500. The limit of detection, determined for 90 compds., was <0.1 mg/L for 73% of the compds. studied and >1.0 mg/L for 6% of the compds. For method comparisons, 50 successive autopsy urine samples were

analyzed by this method, and the results confirmed by **gas** chromatog./mass spectrometry (GC/MS). Findings for parent drugs were consistent with both methods; in addition, LC/TOFMS regularly revealed apparently correct findings for metabolites not shown by GC/MS. Mean and median mass accuracy by LC/TOFMS was 7.6 and 5.4 ppm, resp. The procedure proved well-suited for tentative identification without reference substances. The few false positives emphasized the fact that all three parameters, exact mass, retention time, and metabolite pattern, are required for unequivocal identification.

ST forensic drug pesticide metabolite LC TOFMS database

IT Forensic analysis
(drug; toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT Mass spectrometry
Time-of-flight mass spectrometry
(liquid chromatog. combined with; toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT Liquid chromatography
(mass spectrometry combined with; toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT Databases
(monoisotopic masses and LC retention time; toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT Liquid chromatography
(retention index; toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT Drugs
Drugs of abuse
Human
Urine analysis
(toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT Pesticides
(toxicol. screening of drugs, pesticides and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT 50-53-3D, Chlorpromazine, hydroxy derivs. 58-39-9D, Perphenazine, hydroxy derivative 58-40-2D, Promazine, hydroxy derivs. 60-99-1D, Levomepromazine, hydroxy derivative 107-22-2, Ethanedial 113-59-7D, Chlorprothixene, hydroxy derivs. 130-95-0D, Quinine, hydroxy derivs. 146-21-4, Promazine sulfoxide 298-46-4D, Carbamazepine, dihydroxy derivative 519-98-2, 4-Methylaminoantipyrine 969-99-3, Chlorpromazine sulfoxide 1225-64-5, Norchlorpromazine 2095-17-2, Dinorchlorpromazine 2095-21-8, Dinorpromazine 4317-14-0, Amitriptyline N-oxide 7206-76-0, Phenyl ethyl malonamide 7606-29-3, Levomepromazine sulfoxide 10078-25-8 10538-32-6, Northioridazine 16260-06-3, Chlorprothixene sulfoxide 16260-07-4 16260-08-5, Chlorprothixene N-oxide sulfoxide 34834-67-8, Hydroxycotinine 36507-30-9, Carbamazepine-10,11-epoxide 37517-30-9, Acebutolol 42399-40-6, Deacetyldiltiazem 59878-63-6, Norzopiclone 61337-68-6, Normirtazapine 62498-69-5, Dinorcitalopram 66357-25-3 71936-92-0, Normianserin 73851-70-4, Ranitidine S-oxide 73857-20-2, Ranitidine N-oxide 78549-61-8, 3-Hydroxyquinine **83891-03-6**, Norfluoxetine 84903-78-6, O-Desmethyldiltiazem 86408-42-6, O-Desmethyldeacetylnordiltiazem 86408-44-8 86408-45-9 93413-62-8, O-Desmethylvenlafaxine 122619-90-3, Deacetyldiltiazem N-oxide 149289-30-5, Norvenlafaxine 161696-76-0 625418-06-6, Hydroxypindolol
RL: ANT (Analyte); ANST (Analytical study)

(toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, analysis 50-33-9, Phenylbutazone, analysis 50-36-2, Cocaine 50-37-3, LSD 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, analysis 50-60-2, Phentolamine 51-06-9, Procainamide 51-34-3, Scopolamine 51-55-8, Atropine, analysis 52-53-9, Verapamil 52-86-8, Haloperidol 53-86-1, Indomethacin 54-05-7, Chloroquine 54-11-5, Nicotine 54-85-3, Isoniazide 56-54-2, Quinidine 57-24-9, Strychnine 57-27-2, Morphine, analysis 57-41-0, Phenytoin 57-42-1, Pethidine 57-53-4, Meprobamate 58-08-2, Caffeine, analysis 58-15-1, Aminophenazone 58-25-3, Chlordiazepoxide 58-32-2, Dipyridamole 58-38-8, Prochlorperazine 58-39-9, Perphenazine 58-40-2, Promazine 58-55-9, Theophylline, analysis 58-73-1, Diphenhydramine 59-26-7, Nikethamide 59-32-5, Chloropyramine 59-46-1, Procaine 59-66-5, Acetazolamide 59-99-4, Neostigmine 60-51-5, Dimethoate 60-80-0, Phenazone 60-87-7, Promethazine 60-99-1, Levomepromazine 61-56-3, Sulthiame 61-68-7, Mefenamic acid 62-44-2, Phenacetin 62-67-9, Nalorphine 64-77-7, Tolbutamide 64-86-8, Colchicine 65-45-2, Salicylamide 68-88-2, Hydroxyzine 68-89-3 69-23-8, Fluphenazine 72-14-0, Sulfathiazole 72-44-6, Methaqualone 72-69-5, Nortriptyline 76-42-6, Oxycodone 76-57-3, Codeine 76-58-4, Ethylmorphine 76-99-3, Methadone 77-09-8, Phenolphthalein 77-10-1, Phencyclidine 77-19-0, Dicycloverine 77-23-6, Pentoxiverine 77-36-1, Chlorthalidone 77-37-2, Procyclidine 78-44-4, Carisoprodol 80-77-3, Chlormezanone 81-81-2, Warfarin 82-92-8, Cyclizine 82-93-9, Chlorcyclizine 83-67-0, Theobromine 83-98-7, Orphenadrine 84-22-0, Tetryzoline 84-96-8, Trimeprazine 85-79-0, Cinchocaine 86-21-5, Pheniramine 86-22-6, Brompheniramine 87-00-3, Homatropine 90-84-6, Amfepramone 91-75-8, Antazoline 91-81-6, Tripelenamine 91-84-9, Mepyramine 92-13-7, Pilocarpine 93-14-1, Guaifenesin 93-30-1, Methoxyphenamine 94-20-2, Chlorpropamide 94-24-6, Tetracaine 96-88-8, Mepivacaine 101-40-6, Propylhexedrine 103-90-2, Paracetamol 113-15-5, Ergotamine 113-45-1, Methylphenidate 113-59-7, Chlorprothixene 114-07-8, Erythromycin 115-46-8, Azacyclonol 118-42-3, Hydroxychloroquine 121-75-5, Malathion 122-34-9, Simazine 125-29-1, Hydrocodone 125-33-7, Primidone 125-53-1, Oxyphencyclimine 125-71-3, Dextromethorphan 127-35-5, Phenazocine 128-62-1, Noscapine 129-03-3, Cyproheptadine 130-95-0, Quinine 132-22-9, Chlorpheniramine 134-49-6, Phenmetrazine 137-58-6, Lidocaine 144-11-6, Benzhexol 146-22-5, Nitrazepam 146-48-5, Yohimbine 147-20-6, Diphenylpyraline 153-87-7, Oxypertine 298-46-4, Carbamazepine 298-50-0, Propantheline 298-57-7, Cinnarizine 299-42-3, Ephedrine 300-62-9, Amphetamine 302-27-2, Aconitine 302-33-0, Proadifen 302-40-9, Benactyzine 303-48-0, Norclomipramine 303-49-1, Clomipramine 309-29-5, Doxapram 315-72-0, Opipramol 339-43-5, Carbutamide 357-57-3, Brucine 359-83-1, Pentazocine 362-29-8, Propiomazine 364-62-5, Metoclopramide 390-64-7, Prenylamine 395-28-8, Isoxsuprine 396-01-0, Triamterene 437-38-7, Fentanyl 438-60-8, Protriptyline 439-14-5, Diazepam 443-48-1, Metronidazol 458-24-2, Fenfluramine 465-65-6, Naloxone 466-97-7, Normorphine 467-15-2, Norcodeine 467-60-7, Pipradrol 467-85-6, Normethadone 469-62-5, Dextropropoxyphene 469-79-4, Ketobemidone 479-92-5, Propyphenazone 486-12-4, Triprolidine 486-16-8, Carbinoxamine 486-56-6, Cotinine 493-80-1, Histapyrrodine 493-92-5, Prolintane 500-92-5, Proguanil 509-67-1, Pholcodine 514-65-8, Biperiden 519-09-5, Benzoylecgonine 520-53-6, Psilocin 522-18-9, Chlorbenzoxamine 525-66-6, Propranolol 526-36-3, Xylometazoline 528-92-7, Apronalide 532-03-6, Methocarbamol 533-45-9, Clomethiazole 537-46-2, Methamphetamine 548-73-2, Droperidol 552-79-4, Methylephedrine 561-27-3, Heroin 569-65-3, Meclozine 603-00-9, Proxyphylline 604-75-1, Oxazepam 634-03-7, Phendimetrazine 636-54-4, Clopamide 657-24-9, Metformin 709-55-7, Etilefrine

721-50-6, Prilocaine 738-70-5, Trimethoprim 739-71-9, Trimipramine
768-94-5, Amantadine 835-31-4, Naphazoline 846-49-1, Lorazepam
846-50-4, Temazepam 848-75-9, Lormetazepam 915-30-0, Diphenoxylate
938-73-8, Ethenzamide 963-39-3, Demoxepam 1028-33-7, Pentifylline
1050-79-9, Moperone 1088-11-5, Nordiazepam 1131-64-2, Debrisoquine
1209-98-9, Fencamfamine 1420-55-9, Thiethylperazine 1480-19-9,
Fluanisone 1622-61-3, Clonazepam 1622-62-4, Flunitrazepam 1668-19-5,
Doxepin 1679-76-1, Drofenine 1812-30-2, Bromazepam 1951-25-3,
Amiodarone 2058-52-8, Clothiapine 2062-78-4, Pimozide 2095-20-7,
Norpromazine 2152-34-3, Pemoline 2293-21-2, Nortrimipramine
2470-73-7, Dixyrazine 2530-97-4, Xanthinol 2558-30-7, Norflunitrazepam
2609-46-3, Amiloride 2709-56-0, Flupentixol 2784-73-8 2898-12-6,
Medazepam 2955-38-6, Prazepam 3313-26-6, Tiotixene 3572-43-8,
Bromhexine 3575-80-2, Melperone 3734-33-6, Bitrex 3737-09-5,
Disopyramide 3930-20-9, Sotalol 4205-90-7, Clonidine 4360-12-7,
Ajmaline 4444-42-2 4498-32-2, Dibenzepin 4764-17-4, MDA 4928-02-3,
7-Aminonitrazepam 4959-17-5, 7-Aminoclonazepam 5003-48-5, Benorilate
5560-72-5, Iprindole 5588-33-0, Mesoridazine 5786-21-0, Clozapine
5836-29-3, Coumatetralyl 6452-71-7, Oxprenolol 6493-05-6 6673-35-4,
Practolol 6740-88-1, Ketamine 7020-55-5, Clidinium 7182-53-8,
Butylscopolamine 7416-34-4, Molindone
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

IT 7776-05-8, Thioridazine-5-sulfoxide 10238-21-8, Glibenclamide
10262-69-8, Maprotiline 13523-86-9, Pindolol 13539-59-8, Azapropazone
13655-52-2, Alprenolol 14611-51-9, Selegiline 14759-06-9,
Sulforidazine 14838-15-4, Phenylpropanolamine 14860-49-2, Clobutinol
15574-96-6, Pizotifen 15676-16-1, Sulpiride 15686-51-8, Clemastine
15687-14-6, Embutramide 15793-40-5, Terodiline 16590-41-3, Naltrexone
17560-51-9, Metolazone 17617-23-1, Flurazepam 17692-31-8, Dropropizine
17692-34-1, Etodroxizine 18559-94-9, Salbutamol 19216-56-9, Prazosin
19387-91-8, Tinidazole 19794-93-5, Trazodone 21829-25-4, Nifedipine
22071-15-4, Ketoprofen 22316-47-8, Clobazam 22760-18-5, Proquazone
23031-25-6, Terbutaline 24219-97-4, Mianserine 24526-64-5, Nomifensine
25614-03-3, Bromocriptine 26807-65-8, Indapamide 26839-75-8, Timolol
26864-56-2, Penfluridol 27203-92-5, Tramadol 27892-33-7, Emepronium
28395-03-1, Bumetanide 28721-07-5, Oxcarbazepine 28772-56-7,
Bromadiolone 28911-01-5, Triazolam 28981-97-7, Alprazolam
29094-61-9, Glipizide 29122-68-7, Atenolol 29331-92-8 31828-71-4,
Mexiletine 32501-12-5, Nordextropropoxyphene 34084-50-9,
7-Aminoflunitrazepam 36322-90-4, Piroxicam 36505-84-7, Buspirone
36894-69-6, Labetalol 37306-44-8D, Triazole, hydroxymethyl derivs.
37571-84-9, Amidephrine 37819-98-0, Norlevomepromazine 38194-50-2,
Sulindac 38304-91-5, Minoxidil 38396-39-3, Bupivacaine 38677-85-9,
Flunixin 39860-99-6, Pipotiazine 42045-86-3 42399-41-7, Diltiazem
42542-10-9, MDMA 43200-80-2, Zopiclone 47132-16-1,
(E)-10-Hydroxynortriptyline 47132-19-4, (Z)-10-Hydroxynortriptyline
50679-08-8, Terfenadine 51322-75-9, Tizanidine 51382-91-3,
Norchlorprothixene 51384-51-1, Metoprolol 51481-61-9, Cimetidine
51753-57-2, Fenazepam 51931-66-9, Tilidine 52485-79-7, Buprenorphine
53230-10-7, Mefloquine 53772-83-1, Zuclopenthixol 54063-52-4,
Pitofenone 54063-53-5, Propafenone 54143-55-4, Flecainide
54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 56980-93-9, Celiprolol
57801-81-7, Brotizolam 59467-70-8, Midazolam 59468-90-5,
1-Hydroxymidazolam 59729-33-8, Citalopram 60142-96-3, Gabapentin
61869-08-7, Paroxetine 62498-67-3, Norcitalopram 63659-18-7, Betaxolol
64520-05-4, (E)-10-Hydroxyamitriptyline 66357-35-5, Ranitidine
66722-44-9, Bisoprolol 67018-85-3, Norverapamil 68252-19-7, Pirmenol
68506-86-5, Vigabatrin 68844-77-9, Astemizole 71031-15-7, Cathinone
71125-38-7, Meloxicam 71320-77-9, Moclobemide 71620-89-8, Reboxetine
72402-20-1, (Z)-10-Hydroxyamitriptyline 72509-76-3, Felodipine

72956-09-3, Carvedilol 74103-06-3, Ketorolac 75377-45-6, Nortramadol
75695-93-1, Isradipine 75847-73-3, Enalapril 76547-98-3, Lisinopril
76963-41-2, Nizatidine 78755-81-4, Flumazenil 79516-68-0,
Levocabastine 79617-96-2, Sertraline 79794-75-5, Loratadine
80125-14-0, Remoxipride 80456-81-1, O-Desmethyltramadol 81098-60-4,
Cisapride 81147-92-4, Esmolol 82626-48-0, Zolpidem 83647-97-6,
Spirapril 83799-24-0, Fexofenadine 83881-51-0, Cetirizine
84057-84-1, Lamotrigine 84057-95-4, Ropivacaine 85441-61-8, Quinapril
85650-52-8, Mirtazapine 86386-73-4, Fluconazole 87333-19-5, Ramipril
87848-99-5, Acrivastine 88150-42-9, Amlodipine 88768-40-5, Cilazapril
89365-50-4, Salmeterol 89778-26-7, Toremifene 90729-43-4, Ebastine
92623-85-3, Milnacipran 93413-69-5, Venlafaxine 99614-02-5,
Ondansetron 103628-46-2, Sumatriptan 106266-06-2, Risperidone
106516-24-9, Sertindole 108612-45-9, Mizolastine 111974-69-7,
Quetiapine 114798-26-4, Losartan 115103-54-3, Tiagabine 132539-06-1,
Olanzapine 138853-73-3 139755-83-2, Sildenafil 143558-00-3,
Rocuronium 151319-34-5, Zaleplon 162191-62-0, Nororphenadrine
185502-39-0, Dinortramadol 185502-41-4 625418-07-7
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(toxicol. screening of drugs and metabolites in urine samples with formula-based metabolite identification by liquid chromatog./time-of-flight mass spectrometry)

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; SPE Application note for extraction of acidic, neutral and basic drugs from urine 1997, IST 1044 A
(2) Burlingame, A; Ecotoxicol Environ Saf 1977, V1, P111 CAPLUS
(3) Ehrenthal, W; Acta Pharmacol Toxicol, Suppl 1977, V41, P199 CAPLUS
(4) Gergov, M; J Mass Spectrom 2000, V35, P912 CAPLUS
(5) Gergov, M; Rapid Commun Mass Spectrom 2001, V15, P521 CAPLUS
(6) Kimble, B; J Chromatogr Sci 1974, V12, P647 CAPLUS
(7) Lewis, S; Anal Chem 1979, V51, P1275 CAPLUS
(8) Maizels, M; Anal Chem 2001, V73, P5436 CAPLUS
(9) Marquet, P; Ther Drug Monit 2002, V24, P125 CAPLUS
(10) Marquet, P; Ther Drug Monit 2002, V24, P255 CAPLUS
(11) Michelsen, P; Rapid Commun Mass Spectrom 1999, V13, P2146 CAPLUS
(12) Nielen, M; Rapid Commun Mass Spectrom 2001, V15, P1577 CAPLUS
(13) Sundstrom, I; J Mass Spectrom 2002, V37, P414 CAPLUS
(14) Thevis, M; Biomed Chromatogr 2001, V15, P393 CAPLUS
(15) Thurman, E; J Chromatogr, A 2002, V957, P3 CAPLUS
(16) van Boxclaer, J; Mass Spectrom Rev 2000, V19, P165
(17) Zhang, H; Anal Chem 2000, V72, P3342 CAPLUS
(18) Zhang, H; J Chromatogr, B 2001, V757, P151 CAPLUS
(19) Zhang, H; J Mass Spectrom 2000, V35, P423 CAPLUS
(20) Zhang, N; Anal Chem 2000, V72, P800 CAPLUS

L7 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:308609 CAPLUS
DN 139:316628
ED Entered STN: 23 Apr 2003
TI Effects of orlistat, a lipase inhibitor, on the pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin) in healthy volunteers

AU Zhi, Jianguo; Moore, Rema; Kanitra, Linda; Mulligan, Thomas E.
CS Hoffmann-La Roche, Inc., Nutley, NJ, USA

SO Journal of Clinical Pharmacology (2003), 43(4), 428-435
CODEN: JCPCBR; ISSN: 0091-2700
PB Sage Publications
DT Journal
LA English

CC 1-4 (Pharmacology)

AB To investigate the effect of orlistat on the pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin), the

authors performed double-blind, placebo-controlled, randomized two-period crossover (for fluoxetine and simvastatin) or parallel (for amiodarone) studies in healthy volunteers ages 18 to 65 yr of a body mass index between 18 and 30 kg/m2. During treatment with orlistat or matching placebo for 5 to 13 1/3 days, a single oral dose of highly lipophilic drug was administered, followed by obtaining serial blood samples for measuring plasma (for fluoxetine and simvastatin) or serum (for amiodarone) concns. of the lipophilic drug and its active metabolite. Treatments were compared for the pharmacokinetic parameters AUC0-∞, Cmax, tmax, and t1/2 of highly lipophilic drugs and active metabolites. Anal. of variance was performed to assess the significance of the sequence effect and provide the variance estimate for the 90% confidence intervals. Subjects were also evaluated for adverse events, vital signs, and clin. and laboratory safety.

The absorption of amiodarone (and active metabolite) was significantly reduced by approx. one-quarter using parameters of Cmax and AUC, while no inhibition of absorption was observed for fluoxetine and simvastatin as well as their active metabolites. There were no clin. significant differences in t1/2 and tmax for all three drugs tested. Due to expected **gastrointestinal** adverse events known to occur with orlistat, there was a higher incidence of adverse events under regimen B (highly lipophilic drugs and orlistat) than under regimen A (highly lipophilic drugs and placebo). Other adverse events were sporadic and unremarkable. There were no clin. relevant changes in vital signs or laboratory values. In conclusion, except for amiodarone, there was no effect of orlistat on the pharmacokinetics of highly lipophilic drugs when these drugs were taken concomitantly with orlistat.

ST orlistat lipase inhibitor pharmacokinetics amiodarone fluoxetine simvastatin

IT 5-HT reuptake inhibitors
Antiarrhythmics
Antiobesity agents
Blood plasma
Blood serum
Drug bioavailability
Human
Hypolipemic agents
Intestine
Lipophilicity
Obesity
Urine
(effects of orlistat, a lipase inhibitor, on the pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin) in healthy volunteers)

IT Drug interactions
(pharmacokinetic; effects of orlistat, a lipase inhibitor, on the pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin) in healthy volunteers)

IT 96829-58-2, Orlistat
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of orlistat, a lipase inhibitor, on the pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin) in healthy volunteers)

IT 1951-25-3, Amiodarone 54910-89-3, Fluoxetine 79902-63-9, Simvastatin
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of orlistat, a lipase inhibitor, on the pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin) in healthy volunteers)

IT 9001-62-1, Lipase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; effects of orlistat, a lipase inhibitor, on the

pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin) in healthy volunteers)

IT 83409-32-9, Desethylamiodarone **83891-03-6**, Norfluoxetine 121009-77-6, Simvastatin acid
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(metabolite; effects of orlistat, a lipase inhibitor, on the pharmacokinetics of three highly lipophilic drugs (amiodarone, fluoxetine, and simvastatin) in healthy volunteers)

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; Physicians' Desk Reference 53rd ed 1999
(2) Hartmann, D; Eur J Clin Pharmacol 1996, V50, P421 MEDLINE
(3) Libersa, C; Br J Clin Pharmacol 2000, V49, P373 MEDLINE
(4) Lucas, K; Ann Pharmacother 2001, V35, P314 CAPLUS
(5) Melia, A; Eur J Clin Pharmacol 1998, V54, P773 CAPLUS
(6) Melia, A; J Clin Pharmacol 1995, V35, P840 CAPLUS
(7) Melia, A; J Clin Pharmacol 1996, V36, P352 CAPLUS
(8) Melia, A; J Clin Pharmacol 1996, V36, P647 CAPLUS
(9) Melia, A; J Clin Pharmacol 1996, V36, P654 CAPLUS
(10) Muck, W; Clin Drug Investig 2000, V19, P71 CAPLUS
(11) Oo, C; Clin Drug Investig 1999, V17, P217 CAPLUS
(12) Schuirmann, D; J Pharmacokinet Biopharm 1987, V15, P657 MEDLINE
(13) Weber, C; Eur J Clin Pharmacol 1996, V51, P87 CAPLUS
(14) Zhi, J; Clin Pharmacol Ther 1994, V56, P82 MEDLINE
(15) Zhi, J; J Clin Pharmacol 1995, V35, P521 CAPLUS
(16) Zhi, J; J Clin Pharmacol 1996, V36, P152 CAPLUS
(17) Zhi, J; J Clin Pharmacol 1996, V36, P659 CAPLUS
(18) Zhi, J; J Clin Pharmacol 2002, V42, P1011 CAPLUS

L7 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:133047 CAPLUS
DN 138:163518
ED Entered STN: 21 Feb 2003
TI Improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5
IN Heinrich, Guenther; Kerb, Reinhold
PA Epidauros Biotechnologie AG, Germany
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-4741
ICS A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 3

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003013534	A2	20030220	WO 2002-EP8219	20020723
	WO 2003013534	A3	20031009		
	WO 2003013534	C2	20040429		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1408975 A2 20040421 EP 2002-767255 20020723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRAI EP 2001-117608 A 20010723
EP 2002-11710 A 20020524
WO 2002-EP8219 W 20020723

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003013534	ICM	A61K031-4741
	ICS	A61P035-00

AB The present invention relates to the use of irinotecan or a derivative thereof for the preparation of a pharmaceutical composition for treating colorectal cancer, cervical cancer, **gastric** cancer, lung cancer, malignant glioma, ovarian cancer, and pancreatic cancer in a patient having a genotype with variant alleles of genes involved in irinotecan metabolism, and in particular gene CYP3A5 encoding cytochrome P 450 3A5. Irinotecan (CPT-11) is an analog of the cytotoxic alkaloid camptothecin and is a prodrug of the lipophilic metabolite SN-38 (7-ethyl-10-hydroxycamptothecin). Preferably, a nucleotide deletion, addition and/or substitution comprised by said polynucleotide results in an altered expression of the variant allele compared to the corresponding wild-type allele or an altered activity of the polypeptide encoded by the variant allele compared to the polypeptide encoded by the corresponding wild-type allele. Irinotecan dosage is calculated based on genotype correlated with the risk of toxic reaction.

ST irinotecan cancer therapy human gene genotyping; CYP3A5 genotyping cancer therapy irinotecan; cytochrome P450 CYP3A5 genotyping cancer therapy irinotecan

IT Human groups
(African and Asian; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Grapefruit juice
(CYP3A5 inhibitor; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Gene, animal
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CYP3A5; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Gene, animal
P-glycoproteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MDR1; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Gene, animal
Multidrug resistance proteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MRP1; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Gene, animal
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TOP1; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Gene, animal
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UGT1A1; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Uterus, neoplasm

(cervix; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Intestine, neoplasm
(colorectal; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Genetic polymorphism
(correlated with gene expression and side effects during drug therapy; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Animal
Antitumor agents
Drug resistance
Genotyping (method)
Human
Lung, neoplasm
Mus
Neuroglia, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
(improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT DNA sequences
(of gene alleles involved in irinotecan metabolism; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Protein sequences
(of protein and enzyme variants involved in irinotecan metabolism; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT Susceptibility (genetic)
(to drug toxicity; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497030-84-9 497030-85-0 497030-86-1 497030-87-2 497030-88-3
497030-89-4 497030-90-7 497030-91-8
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(CYP3A5 gene allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 114-07-8, Erythromycin 2751-09-9, Troleandomycin 42399-41-7, DIltiazem
51481-61-9, Cimetidine 54739-18-3, FLuvoxamine 60282-87-3, Gestodene
65277-42-1, Ketoconazole 70458-96-7, Norfloxacin 81103-11-9,
Clarithromycin 83366-66-9, Nefazodone **83891-03-6**,
Norfluoxetine 84371-65-3, Mifepristone 84625-61-6, Itraconazole
85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 116644-53-2,
Mibefradil 127779-20-8, Saquinavir 136817-59-9 150378-17-9,
Indinavir 155213-67-5, Ritonavir 159989-64-7, Nelfinavir
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CYP3A5 inhibitor; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 496954-10-0 496954-11-1 497033-22-4 497033-23-5
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(DNA topoisomerase I allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497031-76-2 497031-77-3 497031-78-4 497031-79-5 497031-80-8
497031-81-9 497031-82-0 497031-83-1 497031-84-2 497031-85-3
497031-86-4 497031-87-5 497031-88-6 497031-89-7 497031-90-0
497031-91-1 497031-92-2 497031-93-3 497031-94-4 497031-95-5
497031-96-6 497031-97-7 497031-98-8 497031-99-9 497032-00-5
497032-01-6 497032-02-7 497032-03-8 497032-04-9 497032-05-0

497032-06-1 497032-07-2 497032-08-3 497032-09-4 497032-10-7
497032-11-8 497032-12-9 497032-13-0 497032-14-1 497032-15-2
497032-16-3 497032-17-4 497032-18-5 497032-19-6 497032-20-9
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497032-31-2 497032-32-3 497032-33-4 497032-34-5 497032-35-6
497032-36-7 497032-37-8 497032-38-9 497032-39-0 497032-40-3
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497032-66-3 497032-67-4 497032-68-5 497032-69-6 497032-70-9
497032-71-0 497032-72-1 497032-79-8 497032-80-1
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MDR1 gene allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497030-92-9 497030-93-0 497030-94-1 497030-95-2 497030-96-3
497030-97-4 497030-98-5 497030-99-6 497031-00-2 497031-01-3
497031-02-4 497031-03-5 497031-04-6 497031-05-7 497031-06-8
497031-07-9 497031-08-0 497031-09-1 497031-10-4 497031-11-5
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497031-72-8 497031-73-9 497031-74-0 497031-75-1
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(MRP1 gene allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497032-73-2 497032-74-3 497032-75-4 497032-76-5 497032-77-6
497032-78-7
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TOP1 gene allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 496953-51-6 496953-52-7 496953-53-8 496953-54-9 496953-55-0
496953-56-1 496953-57-2 496953-58-3 496953-59-4 496953-60-7
496953-61-8 496953-63-0 496953-64-1 496953-65-2 496953-66-3
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497033-00-8 497033-01-9 497033-02-0 497033-03-1 497033-04-2
497033-05-3
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UDP glucosyltransferase 1 allele fragment; improved treatment of

cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497030-22-5 497030-23-6 497030-24-7 497030-25-8 497030-26-9
497030-27-0 497030-28-1 497030-29-2 497030-30-5 497030-31-6
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497030-67-8 497030-68-9 497030-69-0 497030-70-3 497030-71-4
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497030-77-0 497030-78-1 497030-79-2 497030-80-5 497030-81-6
497030-82-7 497030-83-8
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UGT1A1 gene allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 20830-75-5, Digoxin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genotype effect on intestinal uptake-related pharmacokinetics of; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 9046-69-9, UDP glucosyltransferase 102686-80-6, Nifedipine oxidase 143180-75-0, DNA topoisomerase I 336874-97-6, Cytochrome P 450 3A5
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 86639-52-3, SN-38 97682-44-5, Irinotecan
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 496953-86-7 496953-88-9 496953-90-3 496953-92-5 496953-94-7
496953-95-8 496953-97-0 496953-98-1 496953-99-2 496954-00-8
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497033-15-5 497033-16-6 497033-17-7 497033-18-8 497033-19-9
497033-20-2 497033-21-3
RL: ANT (Analyte); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(multidrug resistance protein MRP1 allele fragment; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497052-31-0 497052-32-1 497052-33-2 497052-34-3 497052-35-4
497052-36-5 497052-37-6 497052-38-7 497052-39-8 497052-40-1
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497053-66-4 497053-67-5 497053-68-6 497053-69-7 497053-70-0
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497053-76-6 497053-77-7 497053-78-8 497053-79-9 497053-80-2
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497054-11-2 497054-12-3 497054-13-4 497054-14-5 497054-15-6
497054-16-7 497054-17-8 497054-18-9 497054-19-0 497054-20-3
497054-21-4 497054-22-5 497054-23-6 497054-24-7 497054-25-8
497054-26-9 497054-27-0 497054-28-1 497054-29-2 497054-30-5
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497054-36-1 497054-37-2 497054-38-3 497054-39-4 497054-40-7
497054-41-8 497054-42-9 497054-43-0 497054-44-1 497054-45-2
497054-46-3 497054-47-4 497054-48-5 497054-49-6 497054-50-9
497054-51-0 497054-52-1 497054-53-2 497054-54-3 497054-55-4
497054-56-5 497054-57-6 497054-58-7 497054-59-8 497054-60-1
497054-61-2 497054-62-3 497054-63-4 497054-64-5 497054-65-6
497054-66-7 497054-67-8 497054-68-9 497054-69-0 497054-70-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497054-71-4 497054-72-5 497054-73-6 497054-74-7 497054-75-8
497054-76-9 497054-77-0 497054-78-1 497054-79-2 497054-80-5
497054-81-6 497054-82-7 497054-83-8 497054-84-9 497054-85-0
497054-86-1 497054-87-2 497054-88-3 497054-89-4 497054-90-7
497054-91-8 497054-92-9 497054-93-0 497054-94-1 497054-95-2
497054-96-3 497054-97-4 497054-98-5 497054-99-6 497055-00-2
497055-01-3 497055-02-4 497055-03-5 497055-04-6 497055-05-7
497055-06-8 497055-07-9 497055-08-0 497055-09-1 497055-10-4
497055-11-5 497055-12-6 497055-13-7 497055-14-8 497055-15-9
497055-16-0 497055-17-1 497055-22-8 497055-23-9 497055-24-0
497055-25-1
RL: PRP (Properties)
(unclaimed nucleotide sequence; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

IT 497055-18-2 497055-19-3 497055-20-6 497055-21-7
RL: PRP (Properties)
(unclaimed protein sequence; improved treatment of cancer with irinotecan based on genotyping of human gene CYP3A5 encoding cytochrome P 450 3A5)

L7 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:109510 CAPLUS
DN 139:159428
ED Entered STN: 12 Feb 2003

TI 3D QSAR of serotonin transporter ligands: CoMFA and CoMSIA studies
AU Wellsow, Julia; Machulla, Hans-Juergen; Kovar, Karl-Artur
CS Pharmaceutical Institute, University of Tubingen, Tubingen, 72076, Germany
SO Quantitative Structure-Activity Relationships (2002), 21(6), 577-589
CODEN: QSARDI; ISSN: 0931-8771
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
CC 1-3 (Pharmacology)
AB The main purpose of this study was the investigation of quant. structure-activity relationships of serotonin transporter ligands with regard to the future development of potential new and selective PET radiotracers for the serotonin transporter. A heterogeneous data set of 19 selective and non-selective serotonin reuptake inhibitors was used. Affinity data for both the serotonin transporter and the norepinephrine transporter was available. As a necessary prerequisite for our 3D QSAR studies a reasonable alignment of the compds. was developed using **GASP**. It was based on an existing pharmacophore model. In addition to the widely used CoMFA method, the somewhat newer CoMSIA method was applied. Statistically reliable CoMFA models for both the serotonin transporter (q2=0.538) and the norepinephrine transporter (q2=0.445) were developed, further improving the internal predictability by applying region focusing for the serotonin transporter (q2=0.674). These models were compared with the CoMSIA models for the serotonin and the norepinephrine transporter that yielded comparable cross-validated correlation coeffs. (q2=0.531 and q2=0.502, resp.). Certain structural features that are distinctive of each transporter and important for high binding affinity were identified. Highly comparable results were obtained for CoMFA and CoMSIA. Both methods were applied to elucidate structural requirements for serotonin transporter selectivity. The resulting CoMSIA map provides important information for lead optimization with respect to selectivity enhancement.
ST QSAR CoMFA CoMSIA serotonin transporter ligand pharmacophore
IT Molecular modeling
Pharmacophores
(QSAR of serotonin transporter ligands)
IT QSAR (structure-activity relationship)
(comparative mol. field anal.; QSAR of serotonin transporter ligands)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(norepinephrine transporter; QSAR of serotonin transporter ligands)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serotonin transporter; QSAR of serotonin transporter ligands)
IT 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 72-69-5, Nortriptyline 303-49-1 6640-24-0, m-CPP 19794-93-5, Trazodone 54739-18-3, Fluvoxamine 61869-08-7, Paroxetine 79617-96-2, Sertraline 83366-66-9, Nefazodone 87857-41-8, Desmethylsertraline 93413-44-6 100568-02-3, (S)-Fluoxetine **126924-38-7**, (S)-Norfluoxetine 128196-01-0, (S)-Citalopram 142761-12-4 153707-88-1 301530-74-5
RL: PAC (Pharmacological activity); BIOL (Biological study)
(QSAR of serotonin transporter ligands)
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bohm, M; J Med Chem 1999, V42, P458 MEDLINE
(2) Bush, B; J Comput-Aided Mol Des 1993, V7, P587 CAPLUS
(3) Caruso, F; Acta Crystallogr, Sect C: Cryst Struct Commun 1999, VC55, P1712 CAPLUS
(4) Chang, A; Eur J Pharmacol 1993, V247, P239 CAPLUS
(5) Clark, M; J Comput Chem 1989, V10, P982 CAPLUS
(6) Clark, M; Tetrahedron Comput Methodol 1990, V3, P47 CAPLUS
(7) Clark, R; 13th European Symposium on Quantitative Structure-Activity

Relationships:Rational approaches to drug design 2001, P475 CAPLUS
(8) Cramer, R; 3D QSAR in drug design, Theory methods and applications 1993, P443 CAPLUS
(9) Cramer, R; J Am Chem Soc 1988, V110, P5959 CAPLUS
(10) El-Bermawy, M; Med Chem Res 1992, V2, P290 CAPLUS
(11) Folkers, G; 3D QSAR in drug design, Theory methods and applications 1993, P583 CAPLUS
(12) Gundertofte, K; Computer-assisted lead finding and optimization 1997, P443
(13) Houle, S; Eur J Nucl Med 2000, V27, P1719 CAPLUS
(14) Huang, Y; J Nucl Med 2001, V42(5 Suppl), P105
(15) Humber, L; J Mol Graphics 1985, V3, P84 CAPLUS
(16) Ibers, J; Acta Crystallogr Sect C: Cryst Struct Commun 1999, VC55, P432 CAPLUS
(17) Jones, G; J Comput-Aided Mol Des 1995, V9, P532 CAPLUS
(18) Kim, K; Perspect Drug Disco Des 1998, V12/13/14, P257 CAPLUS
(19) Klebe, G; 3D QSAR in Drug Design:Recent Advances 1998, P87 CAPLUS
(20) Klebe, G; J Med Chem 1994, V37, P4130 CAPLUS
(21) Klein, C; J Pharm Sci 1994, V83, P1253 CAPLUS
(22) Lindberg, U; J Med Chem 1978, V21, P448 CAPLUS
(23) Lindgren, F; J Chemometrics 1994, V8, P349
(24) Lindgren, F; J Chemometrics 1995, V9, P331 CAPLUS
(25) Madding, G; J Heterocycl Chem 1985, V22, P1121 CAPLUS
(26) Matter, H; J Med Chem 1999, V42, P4506 CAPLUS
(27) Muszynski, I; Quant Struct-Act Relat 1999, V18, P342 CAPLUS
(28) Olivier, B; Prog Drug Res 2000, V54, P59 CAPLUS
(29) Owens, M; J Pharmacol Exp Ther 1997, V283, P1305 CAPLUS
(30) Post, M; Acta Crystallogr Sect B 1975, VB31, P1008 CAPLUS
(31) Povlock, S; Neurotransmitter transporters:Structure, function and regulation 1997, P1 CAPLUS
(32) Rudnick, G; Neurotransmitter transporters:Structure, function and regulation 1997, P73 CAPLUS
(33) Rupp, A; Pharm Acta Helv 1994, V68, P235 CAPLUS
(34) Schloss, P; J Psychopharmacol 1998, V12, P115 CAPLUS
(35) Smith, D; Neurosci Biobehav Rev 1986, V10, P37 CAPLUS
(36) Szabo, Z; J Cereb Blood Flow Metab 1995, V15, P798 CAPLUS
(37) Szabo, Z; Synapse 1995, V20, P37 CAPLUS
(38) Thibaut, U; 3D QSAR in drug design, Theory methods and applications 1993, P661 CAPLUS
(39) Tripos Inc; SYBYL Molecular Modeling Software, Version 6.6
(40) Tripos Inc; SYBYL Molecular Modeling Software, Version 6.6, Theory Manual
(41) Wong, G; J Med Chem 1993, V36, P1820 CAPLUS
(42) Yardley, J; J Med Chem 1990, V33, P2899 CAPLUS

L7 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:99023 CAPLUS
DN 139:251
ED Entered STN: 09 Feb 2003
TI Direct stereoselective assay of fluoxetine and norfluoxetine enantiomers in human plasma or serum by two-dimensional **gas**-liquid chromatography with nitrogen-phosphorus selective detection
AU Ulrich, Sven
CS Institute of Clinical Pharmacology, University Hospital Magdeburg, Magdeburg, D-39120, Germany
SO Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 783(2), 481-490
CODEN: JCBAAI; ISSN: 1570-0232
PB Elsevier Science B.V.
DT Journal
LA English
CC 1-1 (Pharmacology)
AB A method was developed and validated for the direct enantioselective assay of fluoxetine and norfluoxetine in human plasma or serum by two-dimensional capillary **gas**-liquid chromatog. (GC). A Rtx-1

fused-silica capillary (15 m+0.25 mm I.D., 1.0 μm film thickness) and a hydrodex-β-6-TBDM fused-silica capillary (25 m+0.25 mm I.D., 0.25 μm film thickness) were used. A three-step liquid-liquid extraction was used for sample preparation with fluvoxamine and nisoxetine as internal stds. The method provided linear calibration between about 5 and 250 ng/mL for (R)- and (S)-fluoxetine as well as 15 and 250 ng/mL for (R)- and (S)-norfluoxetine. The limits of detection were about 1.5 and 6 ng/mL, resp. Intra-day precision (coefficient of variation) was estimated as being between 5.4 and 12.7% at plasma levels of 25, 100 and 200 ng/mL for the four enantiomers. Inter-day precision was between 5.3 and 9.1% at 100 ng/mL. The enantioselective separation of some racemic psychopharmaceuticals was tested with various cyclodextrin GC-capillaries. Advantages and disadvantages of direct enantioselective GC are discussed for the assay of racemic psychopharmaceuticals. Samples from a patient who was treated with racemic fluoxetine were measured. In agreement with literature, plasma levels of the (R)-enantiomers of fluoxetine and norfluoxetine were considerably decreased in comparison to the (S)-enantiomers.

ST fluoxetine norfluoxetine enantiomer blood **gas** liq chromatog

IT Blood analysis
Gas chromatography
Human
(direct stereoselective assay of fluoxetine and norfluoxetine enantiomers in human plasma or serum by two-dimensional **gas** -liquid chromatog. with nitrogen-phosphorus selective detection)

IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine 100568-02-3, (S)-Fluoxetine 100568-03-4, (R)-Fluoxetine **126924-38-7**, (S)-Norfluoxetine **130194-43-3**, (R)-Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(direct stereoselective assay of fluoxetine and norfluoxetine enantiomers in human plasma or serum by two-dimensional **gas** -liquid chromatog. with nitrogen-phosphorus selective detection)

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Altamura, A; Clin Pharmacokinet 1994, V26, P201 MEDLINE
(2) Amsterdam, J; Am J Psychiatry 1997, V154, P963 MEDLINE
(3) Baumann, P; Clin Pharmacokinet 1996, V31, P444 CAPLUS
(4) Bicchi, C; J Chromatogr A 1999, V843, P99 CAPLUS
(5) Cheer, S; Drugs 2001, V61, P81 CAPLUS
(6) Davies, N; J Chromatogr B 1997, V691, P229 CAPLUS
(7) Eap, C; J Chromatogr B 1995, V669, P271 CAPLUS
(8) Eap, C; J Chromatogr B 1996, V682, P265 CAPLUS
(9) Eap, C; J Clin Psychopharmacol 2001, V21, P330 CAPLUS
(10) Fontanille, P; J Chromatogr B 1997, V692, P337 CAPLUS
(11) Gram, L; N Engl J Med 1994, V331, P1354 CAPLUS
(12) Han, S; Biomed Chromatogr 1997, V11, P259 CAPLUS
(13) Knoche, B; Chirality 1996, V8, P30 CAPLUS
(14) Konig, W; J High Resolut Chromatogr 1997, V20, P55 CAPLUS
(15) Kosel, M; J Chromatogr B 1998, V719, P234 CAPLUS
(16) Mosandl, A; J Chromatogr 1992, V624, P267 CAPLUS
(17) Peyton, A; Pharm Res 1991, V8, P1528 CAPLUS
(18) Potts, B; J Liq Chromatogr 1992, V15, P665 CAPLUS
(19) Reepmeyer, J; Chirality 1996, V8, P11 CAPLUS
(20) Schramm, T; J Chromatogr B 1993, V616, P39 CAPLUS
(21) Torok-Both, G; J Chromatogr B 1992, V579, P99 CAPLUS
(22) Ulrich, S; J Chromatogr B 1996, V685, P81 CAPLUS
(23) Ulrich, S; J Pharm Biomed Anal 1996, V14, P441 CAPLUS
(24) Yee, L; J Anal Toxicol 2000, V24, P651 CAPLUS

L7 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:669216 CAPLUS
DN 138:164923
ED Entered STN: 05 Sep 2002

TI Bile analysis of drugs in postmortem cases

AU Vanbinst, R.; Koenig, J.; Di Fazio, V.; Hassoun, A.

CS St-Luc Hospital, Laboratory of Toxicology, Universite Catholique de Louvain, Brussels, 1200, Belg.

SO Forensic Science International (2002), 128(1-2), 35-40
CODEN: FSINDR; ISSN: 0379-0738

PB Elsevier Science Ireland Ltd.

DT Journal

LA English

CC 4-2 (Toxicology)

AB Bile is, in certain cases, collected together with blood from different sites (heart, brain, femoral), urine and other organs or matrixes. This study reports comparative results obtained from the anal. of blood and bile for different drugs found: acetaminophen, amphetamine and related compds., several antidepressants, several benzodiazepines, cocaine and its metabolites, dextropropoxyphene and its metabolite, hydroxyzine, methadone and metabolite, morphine and codeine, levomepromazine, thioridazine, propranolol, tramadol and its metabolite. Several findings are presented: There were no significant differences in the levels of the compds. among the samples of blood obtained from different sites. Levels in bile are generally several fold higher than those in blood. The mean bile to blood ratios vary from about 1 (for acetaminophen, amphetamine) to about 2000 (for desmethylclobazam). In certain cases (16 over 44), although the drug or its metabolite was not detected in blood from different sites, it was detected in bile. As other authors had advocated, it is very useful to ask the pathologist to take the gall bladder with its contents together with the other samples, in order that the sample of bile can be used in the comprehensive toxicol. anal. and therefore be complementary to the other fluids or matrixes. An addnl. advantage for using bile is that the concns. of drugs or their metabolites are generally several fold higher than their blood concns.

ST drug screening bile forensic medicine postmortem

IT Drugs of abuse
(abuse of; drug screening in bile compared with blood, urine, and **gastric** content in forensic postmortem cases)

IT Antidepressants
Bile
Blood
Cadaver
Drug screening
Forensic chemistry
Human
Stomach content
Urine
(drug screening in bile compared with blood, urine, and **gastric** content in forensic postmortem cases)

IT 50-36-2, Cocaine 50-48-6, Amitriptyline 50-52-2, Thioridazine 57-27-2, Morphine, biological studies 60-99-1, Levomepromazine 68-88-2, Hydroxyzine 72-69-5, Nortriptyline 76-57-3, Codeine 76-99-3, Methadone 103-90-2, Acetaminophen 113-53-1, Dosulepine 300-62-9, Amphetamine 439-14-5, Diazepam 469-62-5, Dextropropoxyphene 519-09-5, Benzoylecgonine 525-66-6, Propranolol 529-38-4, Cocaethylene 846-49-1, Lorazepam 1088-11-5, Nordiazepam 1812-30-2, Bromazepam 2894-67-9 7143-09-1, Ecgonine methylester 19794-93-5, Trazodone 22316-47-8, Clobazam 22316-55-8, Desmethylclobazam 27203-92-5, Tramadol 30223-73-5, EDDP 34084-50-9, 7-Amino flunitrazepam 42542-10-9, MDMA 54910-89-3, Fluoxetine 59467-70-8, Midazolam 59468-90-5 66796-40-5, Norpropoxyphene 79617-96-2, Sertraline 80456-81-1, O-Desmethyltramadol **83891-03-6**, Norfluoxetine 87857-41-8, Desmethylsertraline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(drug screening in bile compared with blood, urine, and **gastric** content in forensic postmortem cases)

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Agarwal, A; J Anal Toxicol 1996, V20, P61 CAPLUS
(2) Anon; Medical Toxicology, Diagnosis and Treatment of Human Poisoning 1988, P1234
(3) Bailey, C; Endocrinol Exp 1976, V10, P101 CAPLUS
(4) Brauer, R; J Am Med Assoc 1959, V169, P1462 CAPLUS
(5) Brewster, D; Xenobiotica 1981, V11, P189 CAPLUS
(6) Clevenger, C; J Anal Toxicol 1991, V15, P151 MEDLINE
(7) Gaulier, J; J Forensic Sci 2000, V45, P226 MEDLINE
(8) Kaye, C; J Pharm Pharmacol 1976, V28, P449 CAPLUS
(9) Kintz, P; J Anal Toxicol 1997, V21, P70 CAPLUS
(10) Klaassen, C; Pharm Rev 1984, V36, P1 CAPLUS
(11) Mahon, W; Clin Pharm Ther 1976, V19, P443 CAPLUS
(12) Pounder, D; Forensic Sci Int 1990, V45, P253 MEDLINE
(13) Prouty, R; Proceedings of the 24th International Meeting of TIAFT 1987, P1
(14) Rollins, D; Clin Pharmacokinet 1979, V4, P368 CAPLUS
(15) Sellman, R; Acta Pharmacol Toxicol 1975, V37(3), P242 CAPLUS
(16) Tracqui, A; J Anal Toxicol 1998, V22, P430 CAPLUS

L7 ANSWER 12 OF 47 CAPLUS
AN 2002:665839 CAPLUS
DN 138:362078
ED Entered STN: 04 Sep 2002
TI Transplacental transfer of citalopram, fluoxetine and their primary demethylated metabolites in isolated perfused human placenta
AU Heikkinen, Tuija; Ekblad, Ulla; Laine, Kari
CS Department of Pharmacology and Clinical Pharmacology, University of Turku, Turku, Finland
SO BJOG (2002), 109(9), 1003-1008
CODEN: BIOGFQ; ISSN: 1470-0328
PB Elsevier Science Ltd.
DT Journal
LA English
CC 1-2 (Pharmacology)
AB The objective of this study was to investigate the transplacental transfer and the effects of protein binding on the transfer of citalopram, desmethylcitalopram, fluoxetine and desmethylfluoxetine in the isolated perfused human placenta model. Fifteen term human placentas were obtained immediately after delivery with maternal consent and a 2-h non-recirculating perfusion cycle of a single placental cotyledon was set up. Citalopram (1230 nmol/L) and desmethylcitalopram (600 nmol/L) or fluoxetine (1455 nmol/L) and desmethylfluoxetine (1525 nmol/L) were added to the maternal reservoir and their appearance in the fetal circulation was followed by repeated measurements. To investigate the effect of protein binding on the transfer of citalopram and fluoxetine, nine addnl. perfusions were performed without albumin in the perfusion medium. Citalopram and desmethylcitalopram concns. were measured by reversed-phase high performance liquid chromatog. Fluoxetine and desmethylfluoxetine concns. was measured by **gas** chromatog. and antipyrine (used as a reference compound) concns. spectrophotometrically. The mean (SD) steady-state transplacental transfer (TPTSS%) for citalopram, desmethylcitalopram, fluoxetine and desmethylfluoxetine was 9.1%, 5.6% (P = 0.017 compared with citalopram), 8.7% and 9.1%, resp., calculated as the ratio between the steady-state concns. in fetal venous and maternal arterial sides. The TPTSS%s of citalopram, desmethylcitalopram, fluoxetine and desmethylfluoxetine were 86%, 50%, 88% and 91% of that of freely diffusible antipyrine. The absence of albumin significantly reduced the transfer of citalopram and fluoxetine (TPTSS% 1.1% and 4.8%, resp.) but not the transfer of antipyrine. Thus, citalopram, fluoxetine and desmethylfluoxetine all cross the human placenta, and may, therefore, affect the perinatal outcome of infants exposed to these drugs during pregnancy. The transfer of desmethylcitalopram was significantly lower,

which in the clin. setting may suggest lower fetal exposure of serotonin re-uptake inhibition by citalopram compared with fluoxetine. The presence of albumin was necessary for the transplacental transfer of both citalopram and fluoxetine.

ST transplacental transfer citalopram fluoxetine demethylated metabolite fetus; placenta transfer citalopram fluoxetine desmethylcitalopram desmethylfluoxetine fetus

IT Embryo, animal
(fetus, exposure to drugs; transplacental transfer of citalopram, fluoxetine and their primary demethylated metabolites in isolated perfused human placenta)

IT Albumins, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role in transplacental transfer; transplacental transfer of citalopram, fluoxetine and their primary demethylated metabolites in isolated perfused human placenta)

IT Antidepressants
Biological transport
Human
Placenta
(transplacental transfer of citalopram, fluoxetine and their primary demethylated metabolites in isolated perfused human placenta)

IT 54910-89-3, Fluoxetine 59729-33-8, Citalopram 62498-67-3, Desmethylcitalopram **83891-03-6**, Desmethylfluoxetine
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transplacental transfer of citalopram, fluoxetine and their primary demethylated metabolites in isolated perfused human placenta)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Addis, A; Psychol Med 2000, V30, P89 MEDLINE
(2) Altamura, A; Clin Pharmacokinet 1994, V26, P201 MEDLINE
(3) American Academy of Pediatrics Committee on Drugs; Pediatrics 2000, V105, P880
(4) American College of Obstetricians and Gynecologists; ACOG Technical Bulletin 1993, 182
(5) Bebbington, P; Psychiatr Med 1998, V28, P9 MEDLINE
(6) Bjerkenstedt, L; Eur J Clin Pharmacol 1985, V28, P553 MEDLINE
(7) Bloxam, D; Am J Obstet Gynecol 1986, V155, P382 CAPLUS
(8) Brodie, B; J Biol Chem 1949, V179, P25 CAPLUS
(9) Chambers, C; N Engl J Med 1996, V335, P1010 CAPLUS
(10) Cohen, L; Biol Psychiatry 2000, V48, P996 CAPLUS
(11) Cohen, L; J Clin Psychiatry 1994, V55, P284 MEDLINE
(12) Cohen, L; Psychosomatics 1989, V30, P25 MEDLINE
(13) Coutts, R; Cell Mol Neurobiol 1999, V19, P325 CAPLUS
(14) Cusack, B; Psychopharmacology 1994, V114, P559 CAPLUS
(15) Dancis, J; Am J Physiol 1980, V238, P208
(16) Eaton, B; J Physiol 1993, V463, P141 MEDLINE
(17) Eichelbaum, M; Adv Drug Deliv Rev 1997, V15, P171
(18) Ericson, A; Eur J Clin Pharmacol 1999, V55, P503 CAPLUS
(19) Greenblatt, D; Int J Clin Pharmacol Biopharm 1979, V17, P401 CAPLUS
(20) He, Y; Br J Anaesth 2000, V85, P281 CAPLUS
(21) Heikkinen, T; Psychopharmacology 2001, V153, P450 CAPLUS
(22) Heiskanen, A; Determination of citalopram and desmethylcitalopram in serum by reversed-phase HPLC. Abstract Kemia 93 1993
(23) Hertzberg, T; J Psychosom Obstet Gynaecol 1999, V20, P59 MEDLINE
(24) Hiemke, C; Pharmacol Ther 2000, V85, P11 CAPLUS
(25) Igbal, M; Ann Clin Psychiatry 1999, V11, P237
(26) Isbister, G; Arch Dis Child Fetal Neonatal Ed 2001, V85, PF147 MEDLINE
(27) Kessler, R; J Affect Disord 1993, V29, P85 MEDLINE
(28) Kulin, N; JAMA 1998, V279, P609 CAPLUS
(29) Marcus, S; Int J Gynecol Obstet 2001, V72, P61 MEDLINE
(30) Mhanna, M; Pediatrics 1997, V100, P158 MEDLINE

(31) Milne, R; Drugs 1991, V41, P450 CAPLUS
(32) Naranjo, C; Int Clin Psychopharmacol 1999, V14(Suppl 2), P35
(33) Nash, J; Clin Chem 1982, V28, P2100 CAPLUS
(34) Nulman, I; N Engl J Med 1997, V336, P258 CAPLUS
(35) Orsulak, P; Ther Drug Monit 1989, V11, P497 CAPLUS
(36) Pastuszak, A; JAMA 1993, V269, P2246 CAPLUS
(37) Pincus, H; JAMA 1998, V279, P526 MEDLINE
(38) Schenker, S; Clin Exp Pharmacol Physiol 1999, V26, P691 CAPLUS
(39) Schneider, H; Am J Obstet Gynecol 1972, V114, P822 CAPLUS
(40) Spencer, M; Pediatrics 1993, V92, P721 MEDLINE

L7 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:310322 CAPLUS
DN 137:304639
ED Entered STN: 25 Apr 2002
TI Effect of maternal fluoxetine administration on uterine blood flow, fetal blood **gas** status, and growth
AU Morrison, Janna Leigh; Chien, Caly; Riggs, Kenneth Wayne; Gruber, Nancy; Rurak, Dan
CS Department of Obstetrics and Gynaecology, British Columbia Research Institute for Children's & Women's Health, Vancouver, BC, V5Z 4H4, Can.
SO Pediatric Research (2002), 51(4), 433-442
CODEN: PEREBL; ISSN: 0031-3998
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 1-11 (Pharmacology)
AB Clin. depression, diagnosed in 5-15% of women during pregnancy, increases the risk of neg. pregnancy outcomes including an increased incidence of low birth weight newborns and preterm delivery. Fluoxetine, a selective serotonin reuptake inhibitor, is often prescribed to treat depression due to its efficacy, high margin of safety, and mild side effects. However, fluoxetine initially increases plasma serotonin concentration, and serotonin causes uterine vasoconstriction in sheep, which could result in fetal hypoxemia. To assess fetal fluoxetine effects, late-gestation pregnant sheep were surgically prepared for the measurement of blood **gases**, heart rate, blood pressure, and uterine artery blood flow (n = 29). Ewes received a 70-mg bolus i.v. infusion of fluoxetine over 2 min in 10 mL of sterile water followed by continuous infusion at a rate of 100 μg/min for 8 d (n = 14), or continuous infusion of sterile water (n = 15). Transient decreases in uterine artery blood flow, fetal Po2, and oxygen saturation were observed within the first 15 min after fluoxetine exposure, which did not return to normal values by 24 h. Fetal pH decreased and Pco2 increased over the first 4 h with a return to normal by 24 h. However, there were no differences in uterine artery blood flow, blood **gas** status, or cardiovascular measures between the control and fluoxetine group over the rest of the 8-d infusion period. Thus, fluoxetine exposure during pregnancy has transient effects on fetal status that may be of developmental consequence if they occur repetitively.
ST fluoxetine uterus circulation fetus blood **gas** growth pregnancy
IT Blood
Blood pressure
Circulation
Heart rate
Ovis aries
Pregnancy
Uterus
(effect of maternal fluoxetine administration on uterine blood flow and fetal blood **gas** status and growth)
IT Embryo, animal
(fetus; effect of maternal fluoxetine administration on uterine blood flow and fetal blood **gas** status and growth)

IT Blood plasma
(maternal and fetal plasma fluoxetine levels after maternal administration)
IT 124-38-9, Carbon dioxide, biological studies 7782-44-7, Oxygen, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of maternal fluoxetine administration on uterine blood flow and fetal blood **gas** status and growth)
IT 54910-89-3, Fluoxetine
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of maternal fluoxetine administration on uterine blood flow and fetal blood **gas** status and growth)
IT **83891-03-6**, Norfluoxetine
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(maternal and fetal plasma norfluoxetine levels after maternal fluoxetine administration)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Addis, A; Psychol Med 2000, V30, P89 MEDLINE
(2) Alvarez, J; Clin Pharmacol Ther 1999, V66, P617 CAPLUS
(3) Alvarez, J; Eur Neuropsychopharmacol 1999, V10, P31 CAPLUS
(4) Bell, A; Am J Physiol 1986, V250, PE538 CAPLUS
(5) Benfield, P; Drugs 1986, V32, P481 CAPLUS
(6) Berman, W; Biol Neonate 1978, V33, P225 CAPLUS
(7) Blier, P; Biol Psychiatry 1998, V44, P313 CAPLUS
(8) Bocking, A; J Dev Physiol 1991, V16, P45 MEDLINE
(9) Boddy, K; J Physiol 1974, V243, P599 MEDLINE
(10) Chambers, C; N Engl J Med 1996, V335, P1010 CAPLUS
(11) Clark, K; Life Sci 1980, V27, P2655 CAPLUS
(12) Cohen, L; Biol Psychiatry 2000, V48, P996 CAPLUS
(13) Giussani, D; Am J Physiol 1997, V273, PH2351 CAPLUS
(14) Goldstein, D; J Clin Psychopharmacol 1995, V15, P417 MEDLINE
(15) Hedriana, H; J Soc Gynecol Investig 1995, V2, P727 MEDLINE
(16) Hiemke, C; Pharmacol Ther 2000, V85, P11 CAPLUS
(17) Karlsson, C; Gynecol Obstet Invest 1999, V47, P102 CAPLUS
(18) Kim, J; AAPS PharmSci 1999, V1, PS96
(19) Kim, J; Pharm Res 1995, V12, Ps22
(20) Lawrenson, R; J Affect Disord 2000, V59, P149 MEDLINE
(21) Lemberger, L; J Clin Psychiatry 1985, V46, P14 CAPLUS
(22) Llanos, A; Am J Obstet Gynecol 1986, V155, P893 MEDLINE
(23) Misri, S; Can J Psychiatry 2000, V45, P285 MEDLINE
(24) Nulman, I; N Engl J Med 1997, V336, P258 CAPLUS
(25) Ortiz, J; J Pharmacol 1992, V105, P941 CAPLUS
(26) Pastuszak, A; JAMA 1993, V269, P2246 CAPLUS
(27) Rurak, D; J Pharmacol Exp Ther 1988, V247, P271 CAPLUS
(28) Shinozuka, N; Am J Obstet Gynecol 1999, V180, P1202 CAPLUS
(29) Shinozuka, N; J Soc Gynecol Investig 2000, V7, P108A
(30) Slater, J; Res Vet Sci 1981, V31, P224 CAPLUS
(31) Tan, W; PhD thesis, University of British Columbia 1997, P154
(32) Towell, M; Am J Obstet Gynecol 1987, V157, P1550 CAPLUS
(33) Weissman, M; Science 1995, V269, P799 CAPLUS
(34) Yaffe, H; J Dev Physiol 1987, V9, P325 MEDLINE

L7 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:377581 CAPLUS
DN 133:159587
ED Entered STN: 07 Jun 2000
TI Methods for the determination of seven selective serotonin reuptake inhibitors and three active metabolites in human serum using high-performance liquid chromatography and **gas** chromatography
AU Lacassie, E.; Gaulier, J.-M.; Marquet, P.; Rabatel, J.-F.; Lachatre, G.
CS Department of Pharmacology and Toxicology, University Hospital, Limoges,

87042, Fr.
SO Journal of Chromatography, B: Biomedical Sciences and Applications (2000), 742(2), 229-238
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
CC 1-1 (Pharmacology)
AB This paper describes a set of simple and sensitive multiresidue methods for the determination of the specific serotonin reuptake inhibitors (SSRIs) used as antidepressant drugs, and some of their resp. active metabolites in human serum. It involves liquid-liquid extraction procedures followed by **gas** chromatog. coupled to nitrogen phosphorus detection or isocratic reversed-phase high-performance liquid chromatog. combined with fluorescence detection (HPLC-FL), depending on the analytes. Extraction recoveries were between 71 and 96% for the eight SSRIs and their metabolites analyzed by GC and between 41 and 77% for the two of them analyzed by HPLC. Limits of detection (LODs) and limits of quantitation (LOQs) ranged, resp., from 2.5 to 5 μg/l and from 10 to 20 μg/l. Intra-assay and inter-assay precision was studied at three and four concentration levels, resp., and was less than 19% for all compds. Accuracy was also satisfactory for all. An excellent linearity was observed from the LOQs up to 1000 μg/l for milnacipram and paroxetine and from each LOQ up to 400 mg/l for the other compds. The performance of the methods described thus allows the therapeutic drug monitoring of the currently commercialized SSRIs.
ST serotonin reuptake inhibitor blood analysis HPLC; antidepressant blood analysis **gas** chromatog HPLC
IT Blood analysis
Gas chromatography
HPLC
(methods for determination of seven selective serotonin reuptake inhibitors and three active metabolites in human serum using high-performance liquid chromatog. and **gas** chromatog.)
IT 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 59729-33-8, Citalopram 61869-08-7, Paroxetine 62498-67-3, Desmethylcitalopram 79617-96-2, Sertraline **83891-03-6**, Norfluoxetine 87857-41-8, Desmethylsertraline 92623-85-3, Milnacipran 93413-69-5, Venlafaxine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(methods for determination of seven selective serotonin reuptake inhibitors and three active metabolites in human serum using high-performance liquid chromatog. and **gas** chromatog.)
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Akerman, K; Ther Drug Monit 1998, V20, P25 CAPLUS
(2) Baumann, P; Clin Pharmacokinet 1996, V31, P444 CAPLUS
(3) Brett, M; J Chromatogr B 1987, V419, P438 CAPLUS
(4) Caccia, S; Clin Pharmacokinet 1998, V34, P281 CAPLUS
(5) Clement, E; J Chromatogr B 1998, V2, P303
(6) Eap, C; J Chromatogr B 1996, V686, P51 CAPLUS
(7) Eap, C; J Chromatogr Sci 1998, V36, P365 CAPLUS
(8) Ferslew, K; J Forensic Sci 1998, V43, P1082 MEDLINE
(9) Fontanille, P; J Chromatogr B 1997, V692, P337 CAPLUS
(10) Goodnough, D; J Pharmacol Toxicol Methods 1995, V34, P143 CAPLUS
(11) Jourdil, N; Clin Chem 1997, V43, P2209 CAPLUS
(12) Lacassie, E; Acta Clin Belg 1999, Suppl 19
(13) Lantz, R; J Chromatogr A 1992, V614, P175
(14) Meineke, I; Ther Drug Monit 1998, V20, P14 CAPLUS

(15) Milner, D; J Anal Toxicol 1998, V22, P545 CAPLUS
(16) Patel, J; J Chromatogr B 1996, V10, P351 CAPLUS
(17) Power, B; Clin Pharmacokinet 1995, V29, P154 CAPLUS
(18) Rogowsky, D; J Chromatogr A 1994, V655, P138 CAPLUS
(19) Rop, P; J Chromatogr A 1990, V527, P226 CAPLUS
(20) Tanaka, E; J Chromatogr A 1997, V692, P405 CAPLUS
(21) Torok-Both, G; J Chromatogr A 1992, V579, P99 CAPLUS

L7 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:309892 CAPLUS
DN 133:99029
ED Entered STN: 14 May 2000
TI Identification of the cytochrome P450 enzymes involved in the metabolism of cisapride: in vitro studies of potential co-medication interactions
AU Bohets, H.; Lavrijsen, K.; Hendrickx, J.; Van Houdt, J.; Van Genechten, V.; Verboven, P.; Meuldermans, W.; Heykants, J.
CS Department of Pharmacokinetics, Janssen Research Foundation, Beerse, B-2340, Belg.
SO British Journal of Pharmacology (2000), 129(8), 1655-1667
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
CC 1-2 (Pharmacology)
AB 1 Cisapride is a prokinetic drug that is widely used to facilitate **gastrointestinal** tract motility. 2 Structurally, cisapride is a substituted piperidinyl benzamide that interacts with 5-hydroxy-tryptamine-4 receptors and which is largely without central depressant or antidopaminergic side-effects. 3 The aims of this study were to investigate the metabolism of cisapride in human liver microsomes and to determine which cytochrome P 450 (CYP) isoenzyme(s) are involved in cisapride biotransformation. Addnl., the effects of various drugs on the metabolism of cisapride were investigated. 4 The major in vitro metabolite of cisapride was formed by oxidative N-dealkylation at the piperidine nitrogen, leading to the production of norcisapride. 5 By using competitive inhibition data, correlation studies and heterologous expression systems, it was demonstrated that CYP3A4 was the major CYP involved. CYP2A6 also contributed to the metabolism of cisapride, albeit to a much lesser extent. 6 The mean apparent Km against cisapride was 8.6 ± 3.5 μM (n = 3). The peak plasma levels of cisapride under normal clin. practice are approx. 0.17 μM; therefore it is unlikely that cisapride would inhibit the metabolism of co-administered drugs. 7 In this in vitro study the inhibitory effects of 44 drugs were tested for any effect on cisapride biotransformation. In conclusion, 34 of the drugs are unlikely to have a clin. relevant interaction; however, the antidepressant nefazodone, the macrolide antibiotic troleandomycin, the HIV-1 protease inhibitors ritonavir and indinavir and the calcium channel blocker mibefradil inhibited the metabolism of cisapride and these interactions are likely to be of clin. relevance. Furthermore, the antimycotics ketoconazole, miconazole, hydroxy-itraconazole, itraconazole and fluconazole, when administered orally or i.v., would inhibit cisapride metabolism
ST P450 isoenzyme cisapride metab drug interaction
IT **Gastrointestinal** motility
Liver
(cytochrome P 450 enzymes involved in cisapride metabolism: potential co-medication interactions)
IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(drug-metabolizing; cytochrome P 450 enzymes involved in cisapride metabolism: potential co-medication interactions)
IT Drug interactions
(metabolic; cytochrome P 450 enzymes involved in cisapride metabolism:

potential co-medication interactions)

IT 54-31-9, Furosemide 56-54-2, Quinidine 81-81-2, Warfarin 114-07-8, Erythromycin 130-95-0, Quinine 154-21-2, Lincomycin 439-14-5, Diazepam 443-48-1, Metronidazole 480-41-1, Naringenin 1951-25-3, Amiodarone 2751-09-9, Troleandomycin 16846-24-5, Josamycin 18323-44-9, Clindamycin 21829-25-4, Nifedipine 22916-47-8, Miconazole 28981-97-7, Alprazolam 42399-41-7, Diltiazem 50679-08-8, Terfenadine 51481-61-9, Cimetidine 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 59467-70-8, Midazolam 61869-08-7, Paroxetine 65277-42-1, Ketoconazole 66357-35-5, Ranitidine 68844-77-9, Astemizole 73590-58-6, Omeprazole 73736-50-2, Desmethylastemizole 79617-96-2, Sertraline 80214-83-1, Roxithromycin 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 83366-66-9, Nefazodone **83891-03-6**, Norfluoxetine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 86386-73-4, Fluconazole 91161-71-6, Terbinafine 112559-91-8, Hydroxy-itraconazole 116644-53-2, Mibefradil 127779-20-8, Saquinavir 150378-17-9, Indinavir 155213-67-5, Ritonavir
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(cytochrome P 450 enzymes involved in cisapride metabolism: potential co-medication interactions)

IT 81098-60-4, Cisapride
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cytochrome P 450 enzymes involved in cisapride metabolism: potential co-medication interactions)

IT 9038-14-6, Monooxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cytochrome P 450 enzymes involved in cisapride metabolism: potential co-medication interactions)

IT 83863-69-8, Norcisapride 86718-75-4 104860-64-2, R 053544 115626-75-0, R 063908 115626-77-2, R 062864 115626-78-3, R 062869
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(cytochrome P 450 enzymes involved in cisapride metabolism: potential co-medication interactions)

IT 9035-51-2, p450, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isoenzymes; cytochrome P 450 enzymes involved in cisapride metabolism: potential co-medication interactions)

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Back, D; Br J Clin Pharmacol 1989, V28, P166 CAPLUS
(2) Bateman, D; Eur J Clin Pharmacol 1986, V30, P205 CAPLUS
(3) Bedford, T; Drug Safety 1996, V15, P167 CAPLUS
(4) Berthou, F; Xenobiotica 1989, V19, P401 CAPLUS
(5) Blatchford, N; Royal Society of Medicine Services International Congress and Symposium Series 1988, V132, P29
(6) Brian, W; Biochemistry 1990, V29, P11280 CAPLUS
(7) Brouwers, J; Drug Safety 1992, V7, P268 CAPLUS
(8) Buchheit, K; Eur J Pharmacol 1991, V205, P203 CAPLUS
(9) Chiba, K; J Pharmacol Exp Ther 1993, V266, P52 CAPLUS
(10) Chiba, M; Drug Metab Dispos 1996, V24, P307 CAPLUS
(11) Ching, M; Biochem Pharmacol 1995, V50, P833 CAPLUS
(12) Daneshmend, T; Clin Pharmacokinet 1988, V14, P13 CAPLUS
(13) Dayer, P; Clin Pharmacol Ther 1989, V45, P34 CAPLUS
(14) Delaforge, M; Biochem Pharmacol 1983, V32, P2309 CAPLUS
(15) Duescher, R; Anal Biochem 1993, V212, P311 CAPLUS
(16) Goldstein, J; Biochemistry 1994, V33, P1743 CAPLUS
(17) Greiff, J; Clin Pharmacokin 1994, V27, P447 CAPLUS
(18) Gross, A; Clin Pharmacol Ther 1999, V64, P395
(19) Guengerich, P; Chem Res Toxicol 1991, V4, P391
(20) Horowitz, M; Gastroenterology 1987, V93, P1899
(21) Janssen, C; J Labelled Compd Radiopharm 1987, V24, P1493 CAPLUS

(22) Kirch, W; Ther Drug Monit 1989, V11, P411 CAPLUS
(23) Kumar, G; J Pharmacol Exp Ther 1996, V277, P423 CAPLUS
(24) Lee, H; Biochem Molec Biol Int 1994, V34, P483 CAPLUS
(25) Lin, J; Drug Metab Dispos 1996, V24, P1111 CAPLUS
(26) Lowry, O; J Biol Chem 1951, V193, P265 CAPLUS
(27) McCallum, R; Drugs 1988, V36, P652 MEDLINE
(28) Meuldermans, W; Drug Metab Dispos 1988, V16, P403 CAPLUS
(29) Miles, J; Biochem J 1990, V267, P365 CAPLUS
(30) Miller, G; Anal Chem 1959, V31, P964 CAPLUS
(31) Miners, J; Biochem Pharmacol 1988, V37, P1137 CAPLUS
(32) Omura, T; J Biol Chem 1964, V239, P2379 MEDLINE
(33) Ono, S; Xenobiotica 1996, V26, P681 CAPLUS
(34) Otton, S; Clin Pharmacol Ther 1993, V53, P401 CAPLUS
(35) Periti, P; Clin Pharmacokin 1992, V23, P106 CAPLUS
(36) Peter, R; Chem Res Toxicol 1990, V3, P566 CAPLUS
(37) Pichard, L; Drug Metab Dispos 1990, V18, P595 CAPLUS
(38) Ramirez, B; Alimentary Pharmacol Ther 1993, V7, P5 MEDLINE
(39) Riley, R; Biochem Pharmacol 1990, V39, P1951 CAPLUS
(40) Rowbotham, D; Br J Anaesth 1991, V67, P421 MEDLINE
(41) Shaw, P; Biochem J 1989, V263, P653 CAPLUS
(42) Shulman, R; J Pediatr Gastroenterol Nutr 1996, V23, P395 MEDLINE
(43) Sutton, D; J Pharmacol Exp Ther 1997, V282, P294 CAPLUS
(44) Tassaneeyakul, W; J Pharmacol Exp Ther 1993, V265, P401 CAPLUS
(45) Thomas, A; Pharmacotherapy 1998, V18, P381 MEDLINE
(46) Uges, D; Pham Weekbl 1996, V130, P180
(47) Van Haarst, A; Clin Pharmacol Ther 1998, V64, P542 CAPLUS
(48) Verlinden, M; Excerpta Medica 1988, P30
(49) Von Moltke, L; J Clin Psychopharmacol 1995, V15, P125 MEDLINE
(50) Walker, A; Amer J Med 1999, V107, P356 MEDLINE
(51) Ward, S; J Steroid Biochem Molec Biol 1993, V46, P235 CAPLUS
(52) Wiseman, L; Drugs 1994, V47, P116 MEDLINE
(53) Wysowski, D; N Engl J Med 1996, V335, P290 MEDLINE
(54) Yun, C; Am Soc Pharmacol Exp Ther 1991, V40, P679 CAPLUS

L7 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:338924 CAPLUS
DN 131:153405
ED Entered STN: 03 Jun 1999
TI The stereoselective metabolism of fluoxetine in poor and extensive metabolizers of sparteine
AU Fjordside, Lene; Jeppesen, Unni; Eap, C. B.; Powell, K.; Baumann, Pierre; Brosen, Kim
CS Department of Clinical Pharmacology, Institute of Medical Biology, Odense University, Odense, DK-5000, Den.
SO Pharmacogenetics (1999), 9(1), 55-60
CODEN: PHMCEE; ISSN: 0960-314X
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 1-2 (Pharmacology)
AB The selective serotonin reuptake inhibitor fluoxetine is administered as a racemic mixture, and R- and S-fluoxetine are metabolized in the liver by N-demethylation to R- and S-norfluoxetine, resp. R- and S-fluoxetine and S-norfluoxetine are equally potent selective serotonin reuptake inhibitors, but R-norfluoxetine is 20-fold less potent in this regard. Racemic fluoxetine and norfluoxetine are potent inhibitors of cytochrome P 450 (CYP) 2D6 in vivo and in vitro and recent studies in vivo have shown that racemic fluoxetine is metabolized by CYP2D6. The primary aim of the present study was to investigate the stereoselective metabolism of fluoxetine and norfluoxetine by CYP2D6 in vivo. A single oral dose of fluoxetine (60 mg) was administered to six poor and six extensive metabolizers of sparteine. Blood samples were collected during 6 wk for poor metabolizers and 3 wk for extensive metabolizers. Once a week a sparteine test was

performed. The R- and S-enantiomers of fluoxetine and norfluoxetine were determined by a stereoselective **gas** chromatog.-mass spectroscopy method. In the poor metabolizers, the oral clearance of R- and S-fluoxetine was 3.0 L/h and 17 L/h, resp., the corresponding values in the extensive metabolizers were 36 L/h and 40 L/h, resp. For both enantiomers, the phenotype difference was statistically significant. In poor metabolizers, the elimination half-lives were 6.9 days and 17.4 days for R- and S-norfluoxetine, resp., and in the extensive metabolizers it was 5.5 days for both enantiomers, a significant phenotypical difference only for S-norfluoxetine. For fluoxetine the elimination half-lives were 9.5 and 6.1 days in poor metabolizers for the R- and S-enantiomer, resp. The corresponding values in the extensive metabolizers were 2.6 and 1.1 days, resp. Also for this parameter, the differences were statistically significant. This study shows that CYP2D6 catalyzes the metabolism of R- and S-fluoxetine and most likely the further metabolism of S-norfluoxetine but not of R-norfluoxetine.

ST fluoxetine stereoselective metab poor metabolizer phenotype

IT Drug metabolism
Genetic polymorphism
Liver
Pharmacokinetics
(stereoselective metabolism of fluoxetine in poor and extensive metabolizers of sparteine)

IT 9035-51-2, Cytochrome P 450, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(2D6; stereoselective metabolism of fluoxetine in poor and extensive metabolizers of sparteine)

IT 90-39-1, Sparteine 100568-02-3, S-Fluoxetine 100568-03-4, R-Fluoxetine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stereoselective metabolism of fluoxetine in poor and extensive metabolizers of sparteine)

IT **126924-38-7**, S-Norfluoxetine **130194-43-3**, R-Norfluoxetine
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(stereoselective metabolism of fluoxetine in poor and extensive metabolizers of sparteine)

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Brosen, K; Br J Clin Pharmacol 1991, V32, P136 MEDLINE
(2) Brosen, K; Selective serotonin re-uptake inhibitors: advances in basic research and clinical practice. 2nd edn 1996, P85
(3) Eap, C; Journal Chromatogr B: Biomed Appl 1996, V682, P265 CAPLUS
(4) Fuller, R; Neuropharmacology 1992, V31, P997 MEDLINE
(5) Gram, L; N Engl J Med 1994, V331, P1354 CAPLUS
(6) Hamelin, B; Clin Pharmacol Therapeut 1996, V60, P512 CAPLUS
(7) Lemberger, L; J Clin Psychiatry 1985, V46, P14 CAPLUS
(8) Pato, M; J Clin Psychopharmacol 1991, V11, P224 MEDLINE
(9) Stevens, J; J Pharmacol Exp Ther 1993, V266, P964 CAPLUS
(10) Torok Both, G; J Chromatogr Biomed Appl 1992, V579, P99 CAPLUS
(11) Vaughan, D; Am J Psychiatry 1988, V145, P1478 MEDLINE
(12) Vinks, A; Clin Pharmacol Ther 1982, V31, P23 MEDLINE
(13) Wong, D; Acta Pharm Nord 1990, V2, P171 CAPLUS
(14) Wong, D; Neuropsychopharmacology 1993, V8, P337 CAPLUS

L7 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:167579 CAPLUS

DN 131:111700

ED Entered STN: 15 Mar 1999

TI Effects of serotonin re-uptake inhibition on ventilatory control in goats

AU Henderson, Daniel R.; Konkle, Darlene M.; Mitchell, Gordon S.
CS Department of Comparative Biosciences, University of Wisconsin, Madison, WI, USA
SO Respiration Physiology (1999), 115(1), 1-10
CODEN: RSPYAK; ISSN: 0034-5687
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1
AB Fluoxetine (Prozac) inhibits serotonin (5-HT) re-uptake, thereby enhancing serotonergic effects. Since serotonin is known to affect ventilation in a variety of circumstances, the authors investigated the effects of chronic serotonin re-uptake inhibition with fluoxetine on selected ventilatory responses including: eupnea; the hypercapnic ventilatory response at rest; the exercise ventilatory response and repeated trials of hypercapnic exercise. Ventilatory and arterial blood **gases** were measured in goats (n=5) at rest, during steady-state treadmill exercise, and during successive rest/exercise trials with increased respiratory dead space (0.4-0.6 L). Fluoxetine was administered (≥4 wk, 1 mg/kg, SQ, SID) and protocols were repeated. Following fluoxetine, PaCO2 was increased in most conditions studied; however, no differences were seen in exercise PaCO2 regulation or ventilatory responses pre- vs. post-fluoxetine. The authors conclude that chronic fluoxetine slightly depresses respiratory control at rest, but, has minimal effects during exercise or with mild hypercapnia during rest or exercise in goats.
ST serotonin reuptake inhibition fluoxetine breathing
IT Breathing (animal)
Exercise
Hypercapnia
(serotonin re-uptake inhibition by Prozac and effects on ventilatory control in goats)
IT 56296-78-7, Prozac
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(serotonin re-uptake inhibition by Prozac and effects on ventilatory control in goats)
IT 50-67-9, Serotonin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(serotonin re-uptake inhibition by Prozac and effects on ventilatory control in goats)
IT **83891-03-6**, Norfluoxetine
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(serotonin re-uptake inhibition by Prozac and effects on ventilatory control in goats)
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Altamura, A; Clin Pharmacokinet 1994, V26, P201 MEDLINE
(2) Amsterdam, J; Am J Psychiatry 1997, V154, P963 MEDLINE
(3) Bach, K; Respir Physiol 1993, V91, P57 CAPLUS
(4) Barondes, S; Science 1994, V263, P1102 MEDLINE
(5) Beasley, C; Psychopharmacol 1992, V107, P1 CAPLUS
(6) Bianchi, A; Physiol Rev 1995, V75, P1 CAPLUS
(7) Blier, P; Naunyn-Schmiedebergs Arch Pharmacol 1988, V337, P246 CAPLUS
(8) Bonham, A; Respir Physiol 1995, V101, P219 CAPLUS
(9) Cain, J; J Clin Psychiat 1992, V53, P272 MEDLINE
(10) Dejours, P; Principles of comparative respiratory physiology 1981
(11) Dempsey, J; Federat Proc 1985, V44, P2260 MEDLINE
(12) Dempsey, J; Regulation of breathing 1995, P1065
(13) Martin, P; J Physiol London 1993, V470, P601 MEDLINE

(14) McCrimmon, D; Regulation of Breathing 1995, P151
(15) Mitchell, G; FASEB J 1995, V2, PA666
(16) Mitchell, G; Funkt Biol Syst 1993, V23, P269
(17) Mitchell, G; J Appl Physiol 1990, V69, P718 MEDLINE
(18) Mitchell, G; J Appl Physiol: Respirat Environ Exercise Physiol 1983, V54, P277 CAPLUS
(19) Montgomery, S; Clin Neuropharmacol 1990, V13((Suppl) 1), P71
(20) Ni, Y; Proc Natl Acad Sci USA 1997, V94, P2036 CAPLUS
(21) Olson, E; J Clin Invest 1979, V64, P689 CAPLUS
(22) Pliska, V; Trends Pharmacol Sci 1994, V15, P178 CAPLUS
(23) Smith, C; Respir Physiol 1983, V54, P331 MEDLINE
(24) Turner, D; J Physiol London 1996, V497, P29P
(25) Wong, D; Life Sci 1995, V57, P411 CAPLUS
(26) Wong, D; Neuropsychopharmacology 1991, V5, P43 CAPLUS

L7 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:639587 CAPLUS
DN 130:47043
ED Entered STN: 09 Oct 1998
TI Sensitive, high-throughput **gas** chromatographic-mass spectrometric assay for fluoxetine and norfluoxetine in human plasma and its application to pharmacokinetic studies
AU Addison, R. S.; Franklin, M. E.; Hooper, W. D.
CS Royal Brisbane Hospital, Department of Medicine, Centre for Studies in Drug Disposition, The University of Queensland, Brisbane, 4029, Australia
SO Journal of Chromatography, B: Biomedical Sciences and Applications (1998), 716(1 + 2), 153-160
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
CC 1-1 (Pharmacology)
AB A sensitive, robust **gas** chromatog.-mass spectrometric assay suitable for use in pharmacokinetic or bioequivalence studies is presented for the selective serotonin reuptake inhibitor, fluoxetine, and its major metabolite, norfluoxetine (N-desmethylfluoxetine). This method employs solid-phase extraction followed by acetylation with trifluoroacetic anhydride and anal. of the derivs. using selected ion monitoring. The lower limit of quantification was 1.0 ng/mL, and the assay was linear for both analytes from 1 to 100 ng/mL. Mean recoveries following solid-phase extraction at concns. of 5.0, 20 and 100 ng/mL were 91% (fluoxetine) and 87% (norfluoxetine). Assay precision (as mean RSD) and accuracy (as mean relative error) for both analytes were tested at the same three nominal concns. and were within 10% in all cases. Anal. of fluoxetine concns. in plasma samples from 18 volunteers following administration of a single 40 mg dose of fluoxetine provided the following pharmacokinetic data (mean): Cmax, 32.73 ng/mL; AUC0-∞, 1627 ng/mL h; Tmax, 3.08 h (median); ke, 0.022 h-1; elimination half-life, 37.69 h.
ST **gas** chromatog mass spectrometry fluoxetine norfluoxetine blood pharmacokinetic
IT Mass spectrometry
(**gas** chromatog. combined with; sensitive and high-throughput **gas** chromatog.-mass spectrometric assay for fluoxetine and norfluoxetine in human plasma and application to pharmacokinetic studies)
IT **Gas** chromatography
(mass spectrometry combined with; sensitive and high-throughput **gas** chromatog.-mass spectrometric assay for fluoxetine and norfluoxetine in human plasma and application to pharmacokinetic studies)
IT Blood analysis
Pharmacokinetics
(sensitive and high-throughput **gas** chromatog.-mass

spectrometric assay for fluoxetine and norfluoxetine in human plasma and application to pharmacokinetic studies)

IT 54910-89-3, Fluoxetine
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(sensitive and high-throughput **gas** chromatog.-mass spectrometric assay for fluoxetine and norfluoxetine in human plasma and application to pharmacokinetic studies)

IT **83891-03-6**, Norfluoxetine
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(sensitive and high-throughput **gas** chromatog.-mass spectrometric assay for fluoxetine and norfluoxetine in human plasma and application to pharmacokinetic studies)

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Baumann, P; Clin Pharmacokinet 1996, V31, P444 CAPLUS
(2) Baumann, P; Int Clin Psychopharmacol 1995, V10, P15
(3) Bergstrom, R; Pharm Res 1990, V7, PS251
(4) Dixit, V; J Chromatogr 1991, V563, P379 CAPLUS
(5) Eap, C; J Chromatogr B 1996, V682, P265 CAPLUS
(6) Eap, C; J Chromatogr B 1996, V686, P51 CAPLUS
(7) Fontanille, P; J Chromatogr B 1997, V692, P337 CAPLUS
(8) Fuller, R; Biochem Pharmacol 1978, V27, P193 CAPLUS
(9) Goodnough, D; J Pharmacol Toxicol Methods 1995, V34, P143 CAPLUS
(10) Karim, A; Clin Pharmacol 1996, V36, P490 CAPLUS
(11) Meineke, I; Ther Drug Monit 1998, V20, P14 CAPLUS
(12) Potts, B; J Liq Chromatogr 1992, V15, P665 CAPLUS
(13) Torok-Both, G; J Chromatogr 1992, V579, P99 CAPLUS
(14) Zuccaro, P; Ther Drug Monit 1998, V20, P20 CAPLUS

L7 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:268471 CAPLUS
DN 128:321927
ED Entered STN: 11 May 1998
TI Preparation of substituted gamma aminobutyric acids as anticonvulsants
IN Bryans, Justin Stephen; Horwell, David Christopher; Kneen, Clare Octavia; Wustrow, David Juergen; Thorpe, Andrew John
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C229-22
ICS A61K031-195; C07C323-58
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817627	A1	19980430	WO 1997-US17997	19971007
	W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9746697	A1	19980515	AU 1997-46697	19971007
	EP 937032	A1	19990825	EP 1997-945516	19971007
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO

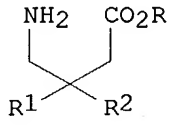
	BR 9712651	A	19991026	BR 1997-12651	19971007
	NZ 334898	A	20000929	NZ 1997-334898	19971007
	JP 2002514187	T2	20020514	JP 1998-519404	19971007
	ZA 9709457	A	19980512	ZA 1997-9457	19971022
	HR 970560	B1	20030228	HR 1997-970560	19971023
	US 6153650	A	20001128	US 1999-254093	19990301
PRAI	US 1996-29601P	P	19961023		
	US 1997-59900P	P	19970924		
	WO 1997-US17997	W	19971007		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9817627	ICM	C07C229-22
	ICS	A61K031-195; C07C323-58

OS MARPAT 128:321927

GI



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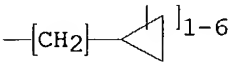

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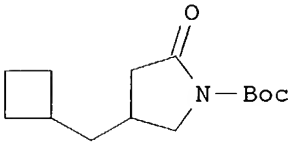
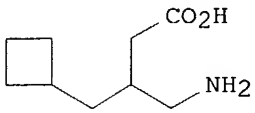


III



IV

AB The title compds. [I; R = H, lower alkyl; R1 = H, lower alkyl; R2 = II, C7-11 alkyl, (CH2)1-4X(CH2)0-4phenyl (wherein X = O, S, NR3; R3 = C1-6 alkyl, C3-8 cycloalkyl, (un)substituted PhCH2, Ph)] and their salts, useful as agents in the treatment of epilepsy, faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, neuropathol. disorders, inflammation, and **gastrointestinal** damage, were prepared Thus, treatment of bromomethylcyclobutane with magnesium turnings in THF followed by the addition of copper bromide dimethylsulfide complex and 1,1-dimethylethyl 2,5-dihydro-2-oxo-1H-pyrrole-1-carboxylate, and the hydrolysis of the intermediate III with 6N HCl afforded the title compound IV.HCl which showed IC50 of 0.407 μM against [3H]gabapentin binding.

ST anticonvulsant gamma aminobutyric acid prepn; hypokinesia gamma aminobutyric acid prepn; faintness attack gamma aminobutyric acid prepn; neurodegenerative disorder gamma aminobutyric acid prepn; antidepressant gamma aminobutyric acid prepn; anxiolytic gamma aminobutyric acid prepn; analgesic gamma aminobutyric acid prepn; antiinflammatory gamma aminobutyric acid prepn; **gastrointestinal** dysfunction gamma aminobutyric acid prepn; digestive system disease aminobutyric acid prepn; panic gamma aminobutyric acid prepn; cranial disorder gamma aminobutyric acid prepn; neuropathol disorder gamma aminobutyric acid prepn

IT Nervous system
(degeneration, treatment of; preparation of substituted gamma aminobutyric acids as anticonvulsants)

IT Digestive tract

(disease, treatment of; preparation of substituted gamma aminobutyric acids as anticonvulsants)

IT Analgesics
Anti-inflammatory agents
Anticonvulsants
Antidepressants
Anxiolytics
(preparation of substituted gamma aminobutyric acids as anticonvulsants)

IT Hypokinesia
(treatment of; preparation of substituted gamma aminobutyric acids as anticonvulsants)

IT 206749-36-2P 206749-37-3P 206749-38-4P 206749-39-5P 206749-40-8P
206749-41-9P 206749-42-0P 206749-43-1P 206749-44-2P 206749-45-3P
206749-46-4P 206749-47-5P 206749-48-6P 206749-49-7P 206749-50-0P
206749-51-1P 206749-52-2P **206749-53-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted gamma aminobutyric acids as anticonvulsants)

IT 104-53-0, Hydrocinnamaldehyde 867-13-0, Triethyl phosphonoacetate
2566-44-1, 2-Cyclopropylethanol 2605-67-6, Methyl (triphenylphosphoranylidene)acetate 5664-21-1, Cyclohexaneacetaldehyde
17247-58-4, Bromomethylcyclobutane 141293-14-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted gamma aminobutyric acids as anticonvulsants)

IT 56105-19-2P, Cyclopropaneacetaldehyde 129042-95-1P 206749-54-4P
206749-55-5P 206749-56-6P 206749-57-7P 206749-58-8P 206749-59-9P
206749-60-2P 206749-61-3P 206749-62-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted gamma aminobutyric acids as anticonvulsants)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Le G Ped I Im A I Gerzena Le; DE 2317180 A 1974 CAPLUS
(2) Northwestern University; WO 9323383 A 1993 CAPLUS
(3) Satzinger, G; US 4024175 A 1977 CAPLUS

L7 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:26204 CAPLUS
DN 128:132529
ED Entered STN: 16 Jan 1998
TI Screening methods for impurities in multi-sourced fluoxetine hydrochloride drug substances and formulations
AU Wirth, D. D.; Olsen, B. A.; Hallenbeck, D. K.; Lake, M. E.; Gregg, S. M.; Perry, F. M.
CS Lilly Research Laboratories, Eli Lilly Co., Lafayette, IN, 47902, USA
SO Chromatographia (1997), 46(9/10), 511-523
CODEN: CHRGB7; ISSN: 0009-5893
PB Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DT Journal
LA English
CC 64-3 (Pharmaceutical Analysis)
AB Gradient HPLC and **gas** chromatog. were applied as screening methods for determination of impurities in fluoxetine HCl drug substances and formulated products from multiple sources. NMR spectroscopy was also used for identification of excipients and some residual solvents. Thirty potential impurities and excipients were investigated. Several impurities were observed in generic products using gradient HPLC that were not detected with isocratic pharmacopeial methods for fluoxetine HCl. Anal. of drug substance samples and capsule formulations from many different suppliers showed a wide variation in quality which, in many cases, would go undetected using isocratic methods. The quality of the innovator's product and some generic samples was high, but many generic samples

contained high levels of impurities. A new impurity, N-benzyl fluoxetine, was observed in some generic samples at levels as high as 0.9%. The gradient HPLC method was also used for stability studies and established that generic capsules formulated with lactose were less stable under accelerated conditions than those formulated without lactose.

ST fluoxetine impurity formulation stability chromatog screening

IT Drug delivery systems
(capsules; screening methods for impurities in fluoxetine HCl drug substances and formulations)

IT Drug delivery systems
Gas chromatography
HPLC
Impurities
NMR (nuclear magnetic resonance)
(screening methods for impurities in fluoxetine HCl drug substances and formulations)

IT 67-64-1, 2-Propanone, analysis 75-05-8, Acetonitrile, analysis 99-76-3, Methyl paraben 108-10-1, Methyl isobutyl ketone 108-88-3, analysis 141-78-6, Ethyl acetate, analysis
RL: ANT (Analyte); ANST (Analytical study)
(screening methods for impurities in fluoxetine HCl drug substances and formulations)

IT 98-56-6P 402-45-9P 936-59-4P 3506-36-3P 21970-65-0P 23580-89-4P, N-Methyl-3-phenylpropylamine 27152-62-1P 42142-52-9P 54910-89-3P, Fluoxetine 56161-71-8P 56161-72-9P 56225-81-1P, Benzenepropanamine, N,N-dimethyl-γ-[4-(trifluoromethyl)phenoxy]- 60960-88-5P, N-Methylcinnamylamine 74681-55-3P 81347-68-4P **83891-03-6P**, Norfluoxetine 159216-80-5P, Benzenepropanamine, N-methyl-N-phenylmethyl-γ-[4-(trifluoromethyl)phenoxy]- 199188-94-8P 199188-97-1P, N-Formylfluoxetine 202122-30-3P 202122-31-4P 202122-32-5P 202122-33-6P, N-Acetylfluoxetine 202122-34-7P
RL: ANT (Analyte); BYP (Byproduct); FMU (Formation, unclassified); ANST (Analytical study); FORM (Formation, nonpreparative); PREP (Preparation)
(screening methods for impurities in fluoxetine HCl drug substances and formulations)

IT 56-81-5, 1,2,3-Propanetriol, analysis 57-10-3, Hexadecanoic acid, analysis 57-11-4, Octadecanoic acid, analysis 544-63-8, Myristic acid, analysis 557-04-0, Magnesium stearate 9005-25-8, Starch, analysis 14641-93-1, α-Lactose
RL: ANT (Analyte); MOA (Modifier or additive use); ANST (Analytical study); USES (Uses)
(screening methods for impurities in fluoxetine HCl drug substances and formulations)

IT 56296-78-7, Fluoxetine hydrochloride
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(screening methods for impurities in fluoxetine HCl drug substances and formulations)

L7 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:651767 CAPLUS
DN 127:325885
ED Entered STN: 15 Oct 1997
TI Simultaneous identification and quantitation of fluoxetine and its metabolite, norfluoxetine, in biological samples by GC-MS
AU Crifasi, Joseph A.; Le, Nha X.; Long, Christopher
CS Forensic Ttoxicology Lab., St. Louis Univ., St. Louis, MO, 63134, USA
SO Journal of Analytical Toxicology (1997), 21(6), 415-419
CODEN: JATOD3; ISSN: 0146-4760
PB Preston Publications
DT Journal
LA English
CC 1-1 (Pharmacology)

Section cross-reference(s): 4

AB A sensitive method for the the quantitation of fluoxetine and norfluoxetine in biol. samples was developed. Blood, urine, and tissue samples were alkalinized and extracted with N-Bu chloride. The exts. were derivatized with pentafluoropropionic anhydride before **gas** chromatog.-mass spectrometry (GC-MS). Selected ions were monitored at m/z 117 and 294 for fluoxetine; m/z 117, 176, and 280 for norfluoxetine; and m/z 122 and 299 for the internal standard fluoxetine-d5. The within-run and between-run precision as well as recovery were determined for both analytes. The empirical limit of detection was determined to be 12.5 μg/L for both fluoxetine and norfluoxetine, whereas the empirical limit of quantitation was 25 μg/L for both drugs. Calibration curves were linear in the range of 50-1000 μg/L for both analytes. Some drugs that were known or suspected of interfering with high-performance liquid chromatog. and GC methods for fluoxetine and norfluoxetine were tested for interference. This is the only reported method that combines the use of a deuterated internal standard, selected ion monitoring by GC-MS, and derivatization for the identification and quantitation of fluoxetine and norfluoxetine.

ST fluoxetine norfluoxetine blood tissue GC MS; **gas** chromatog mass spectrometry fluoxetine norfluoxetine; forensic chem fluoxetine norfluoxetine GC MS; urine vitreous fluoxetine norfluoxetine GC MS

IT Blood analysis
Brain
Forensic chemistry
Liver
Urine analysis
(simultaneous identification and quantitation of fluoxetine and norfluoxetine in biol. samples by GC-MS)

IT Eye
(vitreous humor; simultaneous identification and quantitation of fluoxetine and norfluoxetine in biol. samples by GC-MS)

IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(simultaneous identification and quantitation of fluoxetine and norfluoxetine in biol. samples by GC-MS)

L7 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:256605 CAPLUS
DN 126:338321
ED Entered STN: 19 Apr 1997
TI Direct analysis of fluoxetine and norfluoxetine in plasma by **gas** chromatography with nitrogen-phosphorus detection
AU Fontanille, P.; Jourdil, N.; Villier, C.; Bessard, G.
CS Laboratoire de Pharmacologie, Centre Hospitalier Universitaire de Grenoble, B.P. 217, F-38043, Grenoble, 9, Fr.
SO Journal of Chromatography, B: Biomedical Sciences and Applications (1997), 692(2), 337-343
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier
DT Journal
LA English
CC 1-1 (Pharmacology)

AB A quant. method for the simultaneous GC resolution and detection of fluoxetine and his metabolite norfluoxetine in human plasma was developed. The procedure required 1.0 mL of plasma, extraction with a mixed organic solvent and injection into a capillary **gas** chromatograph with an OV-1 fused-silica column coupled to a nitrogen-phosphorus detector. The calibration curves were linear over the range 5-3000 ng/mL. The detection limits were 0.3 and 2 ng/mL for fluoxetine and norfluoxetine, resp. The assay is suitable for routine anal.

ST fluoxetine metabolite detn blood **gas** chromatog

IT Blood analysis

Capillary **gas** chromatography
(direct anal. of fluoxetine and its metabolite norfluoxetine in human plasma by **gas** chromatog. with nitrogen-phosphorus detection)

IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(direct anal. of fluoxetine and its metabolite norfluoxetine in human plasma by **gas** chromatog. with nitrogen-phosphorus detection)

L7 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:675173 CAPLUS
DN 125:316157
ED Entered STN: 15 Nov 1996
TI The effect of activated charcoal on the absorption of fluoxetine, with special reference to delayed charcoal administration
AU Laine, Kari; Kivisto, Kari T.; Pelttari, Sirpa; Neuvonen, Pertti J.
CS Dep. Pharmacol. Clinical Pharmacol., Univ. Turku, Turku, Italy
SO Pharmacology & Toxicology (Copenhagen) (1996), 79(5), 270-273
CODEN: PHTOEH; ISSN: 0901-9928
PB Munksgaard
DT Journal
LA English
CC 1-2 (Pharmacology)
Section cross-reference(s): 4
AB The effect of activated charcoal on fluoxetine (40 mg) absorption, with special reference to delayed charcoal administration, was investigated in a randomized study with four parallel groups of eight healthy volunteers. The first group ingested fluoxetine on an empty stomach with water only (control). The second group received 25 g of activated charcoal as a suspension immediately after fluoxetine. The third and fourth groups took fluoxetine with water and received 25 g of charcoal 2 or 4 h after fluoxetine. Timed blood samples were taken and plasma fluoxetine and norfluoxetine concns. were measured by GC for 96 h. When charcoal was administered immediately after fluoxetine, the AUC (0-96 h) fluoxetine was reduced by more than 96% ($P<0.0005$) and the Cmax by more than 98% ($P<0.005$). The reduction in the AUC (0-96 h) and Cmax of norfluoxetine was similar to that of fluoxetine. When the administration of charcoal was delayed 2 or 4 h, there was a non-significant mean reduction of 16% and 23% in the AUC (0-92 h) of fluoxetine. Similarly, the Cmax was not significantly reduced by charcoal given 2 or 4 h later. Also, the half-life of fluoxetine was not significantly reduced (by 25%) by the late administration of charcoal. We conclude that activated charcoal, ingested immediately after fluoxetine, practically completely prevents the **gastrointestinal** absorption of fluoxetine. However, regardless of the relatively slow absorption of fluoxetine, delaying charcoal administration 2-4 h greatly reduces its antidotal efficacy.
ST delayed charcoal fluoxetine norfluoxetine **gastrointestinal** absorption
IT Poisoning
(activated charcoal effect on fluoxetine absorption, with special reference to delayed charcoal administration)
IT Charcoal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(activated charcoal effect on fluoxetine absorption, with special reference to delayed charcoal administration)
IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activated charcoal effect on fluoxetine absorption, with special reference to delayed charcoal administration)

L7 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:599888 CAPLUS

DN 125:240430
ED Entered STN: 09 Oct 1996
TI Distribution of venlafaxine in three postmortem cases
AU Levine, Barry; Jenkins, Amanda J.; Queen, Martin; Jufer, Rebecca; Smialek, John E.
CS Office Chief Medical Examiner, Baltimore, MD, 21201, USA
SO Journal of Analytical Toxicology (1996), 20(6), 502-505
CODEN: JATOD3; ISSN: 0146-4760
PB Preston Publications
DT Journal
LA English
CC 4-2 (Toxicology)
Section cross-reference(s): 1
AB Venlafaxine (V) is a second-generation antidepressant approved for use in the United States in 1993. It is a derivative of phenethylamine and is structurally unrelated to firs- and other second-generation antidepressants. Nevertheless, its mechanism of action is similar to other antidepressants; it inhibits the reuptake of presynaptic norepinephrine and serotonin. Its major routes of elimination involve O and N demethylation. O-Desmethylvenlafaxine (ODV) is biol. active. Therapeutic concns. of V and ODV are approx. 0.2 and 0.4 mg/L, resp. Three cases of drug intoxication involving V are presented. V and ODV were identified by **gas** chromatog.-nitrogen-phosphorus detection after alkaline extraction of the biol. specimen. On an HP-5 colum, V and ODV elute after bupropion and fluoxetine, but prior to the first-generation antidepressants, sertraline, amoxapine, and trazodone. V and ODV were confirmed by full scan electron impact **gas** chromatog.-mass spectrometry. The heart-blood V and ODV concns. (mg/L) in the three cases were 6.6 and 31; 84 and 15, and 44 and 50, resp. In case 1, acetaminophen and diphenhydramine were found in the heart blood at 140 and 2.6 mg/L resp. In case 2, amitriptyline, nortriptyline, and chlordiazepoxide were found in the blood at 2.8, 0.5 and 3.3 mg/L, resp. In each case, the manner of death was suicide.
ST venlafaxine postmortem analysis forensic
IT Death
(postmortem; venlafaxine in three postmortem cases)
IT Antidepressants
Bile
Blood analysis
Chromatography, **gas**
Heart
Kidney
Legal chemistry and medicine
Liver
Mass spectrometry
Urine analysis
(venlafaxine in three postmortem cases)
IT 50-48-6 58-25-3, Chlordiazepoxide 58-73-1, Diphenhydramine 103-90-2, Acetaminophen
RL: ANT (Analyte); ANST (Analytical study)
(forensic; venlafaxine in three postmortem cases)
IT 50-47-5, Desipramine 50-49-7, Imipramine 72-69-5 303-49-1, Clomipramine 1225-56-5, Nordoxepin 1668-19-5, Doxepin 19794-93-5, Trazodone 34911-55-2, Bupropion 54910-89-3, Fluoxetine 61869-08-7, Paroxetine 79617-96-2, Sertraline **83891-03-6**, Norfluoxetine 87857-41-8, Desmethylsertraline
RL: ANT (Analyte); ANST (Analytical study)
(venlafaxine in three postmortem cases)
IT 93413-62-8, o-Desmethylvenlafaxine 93413-69-5, Venlafaxine
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)

(venlafaxine in three postmortem cases)

L7 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:460658 CAPLUS
DN 125:132579
ED Entered STN: 03 Aug 1996
TI Inhibition of rat brain monoamine oxidase [iso]enzymes by fluoxetine and norfluoxetine
AU Holt, Andrew; Baker, Glen B.
CS Neurochemical Res. Unit, Univ. Alberta, Edmonton, AB, T6G 2B7, Can.
SO Naunyn-Schmiedeberg's Archives of Pharmacology (1996), 354(1), 17-24
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer
DT Journal
LA English
CC 1-11 (Pharmacology)
AB The interactions of fluoxetine and norfluoxetine with rat brain monoamine oxidase (MAO)-A and-B were examined by a radiochem. assay method. Fluoxetine and norfluoxetine were competitive inhibitors of MAO-A in vitro, with Ki values of 76.3 μM and 90.5 μM, resp. Both compds. were noncompetitive or uncompetitive inhibitors of MAO-B in vitro. Inhibition of MAO-B was time-dependent and was very slowly reversible by dialysis. IC50 values for inhibiting the metabolism of 50 μM β-phenylethylamine were 17.8 μM (fluoxetine) and 18.5 μM (norfluoxetine). Anal. of the time dependence of MAO-B inhibition by fluoxetine revealed that an initial competitive interaction between the enzyme and the inhibitor (Ki 245 μM) was followed by tight-binding enzyme inactivation (kinact 0.071 min-1). Following administration of fluoxetine (20 mg/kg/day) for 7 days, the cortical concentration of fluoxetine plus norfluoxetine was estimated by **gas**-liquid chromatog. to be 700 μM. Such drug treatment reduced MAO-A activity by 23% in 1:8 cortical homogenates, but not in 1:80 homogenates. Inhibition of MAO-B in 1:8 homogenates was modest (12%) and was not reduced by homogenate dilution The concentration of 5-hydroxyindole-3-acetic acid, measured by HPLC, was reduced by
47% in cortices from drug-treated rats, while concns. of 5-hydroxytryptamine, noradrenaline, dopamine, 3,4-dihydroxyphenylacetic acid and homovanillic acid were unchanged. These results suggest that, following chronic drug administration leading to relatively high tissue concns. of fluoxetine and norfluoxetine, inhibition of either form of MAO would be restricted by competition for the enzyme by intraneuronal amine substrates.
ST brain monoamine oxidase fluoxetine norfluoxetine
IT Antidepressants
Brain
Kinetics, enzymic
(inhibition of brain monoamine oxidase forms by fluoxetine and norfluoxetine)
IT Amines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(biogenic, inhibition of brain monoamine oxidase forms by fluoxetine and norfluoxetine in relation to metabolism of)
IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of brain monoamine oxidase forms by fluoxetine and norfluoxetine)
IT 9001-66-5, Monoamine oxidase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of brain monoamine oxidase forms by fluoxetine and

norfluoxetine)

IT 64-04-0, β-Phenethylamine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of brain monoamine oxidase forms by fluoxetine and norfluoxetine as determined by metabolism of)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-43-4, Adrenaline 54-16-0, 5-HIAA, biological studies 102-32-9, DOPAC 306-08-1, Homovanillic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(inhibition of brain monoamine oxidase forms by fluoxetine and norfluoxetine in relation to metabolism of)

L7 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:459492 CAPLUS
DN 125:184723
ED Entered STN: 03 Aug 1996
TI Simultaneous determination of plasma levels of fluvoxamine and of the enantiomers of fluoxetine and norfluoxetine by **gas** chromatography-mass spectrometry
AU Eap, C. B.; Gaillard, N.; Powell, K.; Baumann, P.
CS Unite de Biochimie et Psychopharmacologie Clinique, Departement Universitaire de Psychiatrie Adulte, Hopital de Cery, Prilly-Lausanne, CH-1008, Switz.
SO Journal of Chromatography, B: Biomedical Applications (1996), 682(2), 265-272
CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier
DT Journal
LA English
CC 1-1 (Pharmacology)
AB A **gas** chromatog.-mass spectrometric method is presented which allows the simultaneous determination of the plasma concns. of fluvoxamine and of the enantiomers of fluoxetine and norfluoxetine after derivatization with the chiral reagent, (S)-(-)-N-trifluoroacetylprolyl chloride. No interference was observed from endogenous compds. following the extraction of plasma samples from six different human subjects. The standard curves were linear over a working range of 10 to 750 ng/mL for racemic fluoxetine and norfluoxetine and of 50 to 500 ng/mL for fluvoxamine. Recoveries ranged from 50 to 66% for the three compds. Intra- and inter-day coeffs. of variation ranged from 4 to 10% for fluvoxamine and from 4 to 13% for fluoxetine and norfluoxetine. The limits of quantitation of the method were found to be 2 ng/mL for fluvoxamine and 1 ng/mL for the (R)- and (S)-enantiomers of fluoxetine and norfluoxetine, hence allowing its use for single dose pharmacokinetics. Finally, by using a steeper gradient of temperature, much shorter anal. times are obtained if one is interested in the concns. of fluvoxamine alone.
ST blood fluvoxamine fluoxetine norfluoxetine GC MS; **gas** chromatog blood fluvoxamine fluoxetine norfluoxetine; mass spectrometry blood fluvoxamine fluoxetine norfluoxetine
IT Blood analysis
(simultaneous determination of plasma levels of fluvoxamine and enantiomers of fluoxetine and norfluoxetine by **gas** chromatog.-mass spectrometry)
IT 54739-18-3, Fluvoxamine 100568-02-3, (S)-Fluoxetine 100568-03-4, (R)-Fluoxetine **126924-38-7**, (S)-Norfluoxetine **130194-43-3**, (R)-Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(simultaneous determination of plasma levels of fluvoxamine and enantiomers of

fluoxetine and norfluoxetine by **gas** chromatog.-mass spectrometry)

L7 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:163353 CAPLUS
DN 124:249602
ED Entered STN: 20 Mar 1996
TI Excretion of fluoxetine and its metabolite, norfluoxetine, in human breast milk
AU Taddio, Anna; Ito, Shinya; Koren, Gideon
CS Department Pediatrics, Hospital Sick Children, Toronto, ON, M5G 1X8, Can.
SO Journal of Clinical Pharmacology (1996), 36(1), 42-7
CODEN: JCPCBR; ISSN: 0091-2700
PB Lippincott-Raven
DT Journal
LA English
CC 1-2 (Pharmacology)
AB A study was conducted to measure breast milk concns. of fluoxetine and its active metabolite, norfluoxetine, excreted in breast milk in a cohort of nursing women using fluoxetine, and to estimate infant dose from nursing. The study included 10 women nursing 11 infants (median age, 185 days). The mean fluoxetine dose was 0.39 mg/kg/day. Each patient manually collected 3 to 6 milk samples throughout a dosing interval. Concns. of fluoxetine and norfluoxetine in milk were measured by **gas**-liquid chromatog. Mothers reported whether they observed adverse effects in their infants. The average infant doses of fluoxetine and norfluoxetine, as estimated for an exclusively breast-fed infant ingesting 1000 mL of milk per day, were 0.077 mg (SD = 0.054 mg) and 0.084 mg (SD = 0.043 mg), resp. The total dose of fluoxetine and norfluoxetine (expressed as fluoxetine equivalent) was 0.165 mg (SD = 0.092 mg), which was equivalent to 10.8% (SD = 2.2%) of the maternal dose, adjusted on a mg/kg basis in a 4-kg infant. No adverse events were reported by mothers in their infants. Approx. one tenth of the adult therapeutic dose of fluoxetine is excreted in breast milk. Although short-term adverse effects in the infant from exposure through nursing were not reported in this cohort, future studies that assess the potential long-term consequences are needed.
ST fluoxetine norfluoxetine excretion breast milk
IT Milk
(human, excretion of fluoxetine and its metabolite norfluoxetine in human breast milk)
IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(excretion of fluoxetine and its metabolite norfluoxetine in human breast milk)

L7 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:915684 CAPLUS
DN 123:329151
ED Entered STN: 14 Nov 1995
TI Simultaneous quantification of fluoxetine, norfluoxetine, and desipramine using **gas** chromatography with nitrogen-phosphorus detection
AU Goodnough, D. B.; Baker, G. B.; Coutts, R. T.
CS Dep. of Psychiatry, Univ. of Alberta, Edmonton, AB, Can.
SO Journal of Pharmacological and Toxicological Methods (1995), 34(3), 143-7
CODEN: JPTMEZ; ISSN: 1056-8719
PB Elsevier
DT Journal
LA English
CC 1-1 (Pharmacology)
AB The combination of fluoxetine (FLU) and desipramine (DMI) has been reported to be useful for the treatment of depression, and these drugs are also known to undergo a metabolic drug-drug interaction because of their

effects on cytochrome P 450 2D6. A procedure that separates these two drugs and norfluoxetine (NFLU), the N-demethylated metabolite of FLU, and that allows simultaneous quantification of their levels would be of value and has been developed in the labs. The procedure involves and initial extraction into Et acetate after basification of the homogenate. The organic phase is retained and taken to dryness; the residue is reconstituted in water and acetylated with acetic anhydride under slightly basic conditions. Et acetate is then used to extract the acetylated compds. from the aqueous medium. The organic layer is taken to dryness and the residue reconstituted in toluene. An aliquot of the solution in toluene is injected directly into a **gas** chromatograph equipped with a nitrogen-phosphorus detector, a fused silica capillary column, and an integrator/printer. Maprotiline is added to the initial homogenate and carried through the procedure as the internal standard The assay is rapid and sensitive and has been applied successfully to liver and brain tissue taken from rats treated with FLU, DMI, or the combination.

ST fluoxetine norfluoxetine desipramine **gas** chromatog liver; brain fluoxetine norfluoxetine desipramine **gas** chromatog

IT Brain
Chromatography, **gas**
Liver
(simultaneous quantification of fluoxetine, norfluoxetine, and desipramine using **gas** chromatog. with nitrogen-phosphorus detection)

IT 50-47-5, Desipramine 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(simultaneous quantification of fluoxetine, norfluoxetine, and desipramine using **gas** chromatog. with nitrogen-phosphorus detection)

L7 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:570276 CAPLUS
DN 121:170276
ED Entered STN: 15 Oct 1994
TI The effects of desipramine and iprindole on levels of enantiomers of fluoxetine in rat brain and urine
AU Aspeslet, Launa J.; Baker, Glen B.; Coutts, Ronald T.; Torok-Both, George A.
CS Fac. Pharm. Pharm. Sci., Univ. Alberta, Edmonton, AB, Can.
SO Chirality (1994), 6(2), 86-90
CODEN: CHRLEP; ISSN: 0899-0042
DT Journal
LA English
CC 1-11 (Pharmacology)
AB The antidepressant fluoxetine (FLU) and its N-demethylated metabolite, norfluoxetine (NFLU), each contains a chiral center. The combination of FLU and desipramine (DMI), another antidepressant, has been reported to be useful in treatment of depression, to dramatically increase plasma levels of DMI and also to produce more rapid β-adrenergic receptor down-regulation in brain than caused by DMI alone. The authors have now begun studies on the effects of this drug combination on the levels of FLU and NFLU enantiomers in the rat. In addition, the combination of FLU and iprindole (IPR) was also investigated. Male Sprague-Dawley rats were treated i.p. with either normal saline vehicle, DMI (5 mg/kg/day), (R,S)-FLU (10 mg/kg/day) or DMI (5 mg/kg/day) + (R,S)-FLU (10 mg/kg/day) for 4 days. Following the last treatment, 24 h urine samples were collected. Rats were sacrificed and brains were removed. For the IPR study, rats were pretreated with either saline of IPR-HCl (11.2 mg/kg) and then treated 1 h later with (R,S)-FLU. After 5 h, the rats were sacrificed and brains were removed. Brain and urine samples were analyzed by **gas** chromatog. with electron-capture detection of free (R)- and (S)-FLU and (R)- and (S)-NFLU after extraction and reaction with

(-)-(S)-N-(trifluoroacetyl)prolyl chloride. The results from the brains of the rats treated with DMI/FLU indicate that levels of the enantiomers of both FLU and NFLU were significantly increased over those seen in the animals receiving (R,S)-FLU alone. In the IPR/FLU treated rats, an increase in the brain levels of both (R)- and (S)-FLU was noted when compared with rats receiving (R,S)-FLU alone; however, there appeared to be no increase in the brain levels of NFLU enantiomers.

ST antidepressant brain urine fluoxetine norfluoxetine enantiomer; brain fluoxetine norfluoxetine enantiomer desipramine iprindole; urine fluoxetine norfluoxetine enantiomer desipramine iprindole; fluoxetine enantiomer brain urine desipramine iprindole; norfluoxetine enantiomer brain urine desipramine iprindole; desipramine brain urine fluoxetine norfluoxetine enantiomer; iprindole brain urine fluoxetine norfluoxetine enantiomer

IT Antidepressants
(desipramine and iprindole, fluoxetine and norfluoxetine levels in brain and urine response to, antidepressant action in relation to)

IT Drug interactions
(synergistic, of antidepressants desipramine and iprindole, with fluoxetine and norfluoxetine)

IT 50-47-5, Desipramine 5560-72-5, Iprindole
RL: BIOL (Biological study)
(fluoxetine and norfluoxetine enantiomers of brain and urine response to, antidepressant action in relation to)

IT 54910-89-3 **83891-03-6** 100568-02-3, (S)-Fluoxetine
100568-03-4 **126924-38-7**, (S)-Norfluoxetine **130194-43-3**
RL: BIOL (Biological study)
(of brain and urine, desipramine and iprindole effect on, synergistic antidepressant action in relation to)

L7 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:419818 CAPLUS
DN 119:19818
ED Entered STN: 24 Jul 1993
TI Determination of fluoxetine and norfluoxetine in human plasma by capillary **gas** chromatography with electron-capture detection
AU Lantz, R. J.; Farid, K. Z.; Koons, J.; Tenbarge, J. B.; Bopp, R. J.
CS Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SO Journal of Chromatography, Biomedical Applications (1993), 614(1), 175-9
CODEN: JCBADL; ISSN: 0378-4347
DT Journal
LA English
CC 1-1 (Pharmacology)
AB A capillary **gas** chromatog. method with 63Ni electron-capture detection is reported for the determination of fluoxetine (Prozac) and its metabolite norfluoxetine in human plasma. A liquid-liquid extraction is used, followed by derivatization with heptafluorobutyric anhydride to increase the sensitivity of detection. A 30 m + 0.25 mm I.D. DB-17 capillary column resolves the compds. from endogenous matrix interferences. The limit of quantitation by this method is 5 ng/mL for each compound Stability studies show that fluoxetine and norfluoxetine are stable in human plasma for up to 96 h at room temperature and up to one year at -20°C.

ST fluoxetine norfluoxetine plasma capillary **gas** chromatog

IT Blood analysis
(fluoxetine and norfluoxetine determination in human, by capillary **gas** chromatog. with electron-capture detection)

IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in human blood plasma by capillary **gas** chromatog. with electron-capture detection)

L7 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:542798 CAPLUS

DN 117:142798
ED Entered STN: 17 Oct 1992
TI Simultaneous determination of fluoxetine and norfluoxetine enantiomers in biological samples by **gas** chromatography with electron-capture detection
AU Torok-Both, George A.; Baker, Glen B.; Coutts, Ronald T.; McKenna, Kevin F.; Aspeslet, Launa J.
CS Fac. Pharm. Pharm. Sci., Univ. Alberta, Edmonton, AB, T6G 2B7, Can.
SO Journal of Chromatography (1992), 579(1), 99-106
CODEN: JOCRAM; ISSN: 0021-9673
DT Journal
LA English
CC 1-1 (Pharmacology)
AB An electron-capture **gas** chromatog. procedure was developed for the simultaneous anal. of the enantiomers of fluoxetine and norfluoxetine. The assay involves basis extraction of these enantiomers from the biol. samples, followed by their conversion to diastereoisomers using the chiral derivatizing reagent (S)-(-)-N-trifluoroacetylprolyl chloride. The method was utilized to detect and measure the quantity of these enantiomers in plasma and urine of patients and in liver and brain tissue of rats treated with (R,S)-fluoxetine.
ST fluoxetine norfluoxetine enantiomer detn **gas** chromatog; biol sample fluoxetine norfluoxetine enantiomer detn
IT Brain, composition
Liver, composition
(fluoxetine and norfluoxetine enantiomers determination in, by **gas** chromatog. with electron-capture detection)
IT Blood analysis
Urine analysis
(fluoxetine and norfluoxetine enantiomers determination in, of humans, by **gas** chromatog. with electron-capture detection)
IT Chromatography, **gas**
(fluoxetine and norfluoxetine enantiomers simultaneous determination in biol.
samples of humans and laboratory animals by)
IT 54910-89-3
RL: ANST (Analytical study)
(determination of enantiomers of, in biol. samples of humans and laboratory animals,
by **gas** chromatog. with electron-capture detection)
IT 100568-02-3, (S)-Fluoxetine 100568-03-4, (R)-Fluoxetine
126924-38-7, (S)-Norfluoxetine **130194-43-3**,
(R)-Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in biol. samples of humans and laboratory animals, by **gas** chromatog. with electron-capture detection)

L7 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:75577 CAPLUS
DN 116:75577
ED Entered STN: 06 Mar 1992
TI The stereospecific determination of fluoxetine and norfluoxetine enantiomers in human plasma by high-pressure liquid chromatography (HPLC) with fluorescence detection
AU Peyton, Albert L.; Carpenter, Russell; Rutkowski, Kathleen
CS Lilly Lab. Clin. Res., Eli Lilly and Co., Indianapolis, IN, 46202, USA
SO Pharmaceutical Research (1991), 8(12), 1528-32
CODEN: PHREEB; ISSN: 0724-8741
DT Journal
LA English
CC 1-1 (Pharmacology)
AB A quant. method for the simultaneous HPLC resolution and detection of the enantiomers of (R,S)-fluoxetine (F) and their metabolites

(R,S)-norfluoxetine (N) in human blood plasma was developed. F is a serotonin uptake inhibitor used in the treatment of depression and is administered as a racemate. After liquid-liquid extraction and derivatization with (R)-naphthylethylisocyanate (NEI), the separation and detection of the resultant diasteriomers were achieved using normal-phase HPLC and fluorescence. The four NEI diastereomers and the internal standard [(-)-N-methyl-γ-(2-methylphenoxy)benzenepropanamine], representing the enantiomers S-F, R-F, S-N, and R-N were resolved within 15 min. The assay for each analyte was linear using two concentration ranges of 1-10 and 10-500 ng/mL of human plasma. The precision and accuracy are reported as the coefficient of variation (%CV) and relative error (%RE). The sum of the chiral HPLC results from plasma samples were compared to the achiral **gas** chromatog./electron capture results. The correlation between these two methods, for total F and N, resulted in r2 values of 0.98 and 0.89, resp. The chiral HPLC method is currently being applied to clin. studies for the evaluation of the enantiomeric disposition of F.

ST fluoxetine norfluoxetine enantiomer blood liq chromatog; HPOC fluoxetine norfluoxetine enantiomer blood

IT Blood analysis
(fluoxetine and norfluoxetine enantiomers determination in human, by HPLC)

IT **126924-38-7**, (S)-Norfluoxetine **130194-43-3**, (R)-Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, as fluoxetine metabolite, in blood plasma of human, by HPLC)

IT 100568-02-3, (S)-Fluoxetine 100568-03-4, (R)-Fluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma of human, by HPLC)

L7 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:135497 CAPLUS
DN 114:135497
ED Entered STN: 19 Apr 1991
TI Biodistribution and metabolism in rats and mice of bucromarone
AU Maurizis, J. C.; Nicolas, C.; Verny, M.; Ollier, M.; Faurie, M.; Payard, M.; Veyre, A.
CS Inst. Natl. Sante Rech. Med. U 71, Clermont-Ferrand, 63005, Fr.
SO Drug Metabolism and Disposition (1991), 19(1), 94-9
CODEN: DMDSAI; ISSN: 0090-9556
DT Journal
LA English
CC 1-2 (Pharmacology)
Section cross-reference(s): 63

AB The metabolism and disposition of bucromarone, labeled with 14C on the chromone group, has been investigated in C3H mice and Wistar rats. Animals received 4.4 mmol/kg, i.v. or orally, of [14C]bucromarone hydrochloride or succinate. More than 90% of the administered radioactivity was excreted in bile. Less than 5 min after i.v. injection, the radioactivity was concentrated in all tissues, and blood concentration became very low as compared with the initial level. After oral administration, no more than 10% of the dose was in the tissues. The discrepancy between the high biliary excretion and the low tissue and blood concns. after oral administration suggested that bucromarone was well absorbed through the **gastrointestinal** tract; but after liver uptake, the drug and its metabolites were excreted in the bile with less than 10% being distributed into the extrahepatic blood. Comparison of the i.v. and oral areas under the plasma 14C-radioactivity concentration-time curves indicated a poor bioavailability of the drug after oral administration. Anal. of the radioactivity content of bile showed that bucromarone was extensively metabolized after administration by both routes. The unchanged bucromarone and three main metabolites, monodesbutylbucromarone,

didesbutylbucromarone, and 2-(3,5-dimethyl-4-hydroxybenzoyl)chromone, amounting to 85% of the bile radioactivity, were identified by HPLC and mass spectrometry. These findings are consistent with dealkylation of the N-dibutyl group, yielding potentially pharmacol. active metabolites monodesbutyl and didesbutyl bucromarone.

ST bucromarone metab bile bioavailability

IT Blood
Blood plasma
Brain, metabolism
Heart, metabolism
Kidney, metabolism
Liver, metabolism
Lung, metabolism
Spleen, metabolism
Stomach, metabolism
(bucromarone distribution in, after oral and i.v. administration)

IT Bile
Feces
Urine
(bucromarone excretion with, bioavailability after oral or i.v. administration in relation to)

IT Drug bioavailability
(of bucromarone, after oral and i.v. administration)

IT Intestine, metabolism
(small, bucromarone distribution in, after oral and i.v. administration)

IT 78371-66-1, Bucromarone 84604-94-4
RL: BIOL (Biological study)
(biodistribution and metabolism of, route of administration in relation to)

IT 67652-27-1 **132732-92-4** 132732-93-5
RL: PROC (Process)
(biodistribution of, as bucromarone metabolite)

IT 6276-54-6, 3-Chloropropylamine hydrochloride
RL: BIOL (Biological study)
(butoxycarbonylation of)

IT 116861-31-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with (dimethylhydroxybenzoyl)chromone)

IT 6940-78-9P, 1-Bromo-4-chlorobutane **132757-89-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 107128-17-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chloropropylamine derivative)

L7 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:135447 CAPLUS
DN 114:135447
ED Entered STN: 19 Apr 1991
TI Solid-phase extraction of fluoxetine and norfluoxetine from serum with **gas** chromatography-electron-capture detection
AU Dixit, Vandana; Nguyen, Hung; Dixit, Vyas M.
CS Varian Sample Prep. Prod., Harbor City, CA, 90710, USA
SO Journal of Chromatography (1991), 563(2), 379-84
CODEN: JOCRAM; ISSN: 0021-9673
DT Journal
LA English
CC 1-1 (Pharmacology)
AB A rapid, selective, and sensitive method is described for the purification and anal. of fluoxetine and norfluoxetine using a solid-phase extraction column and **gas** chromatog.-electron-capture detection. Linear quant. response curves for fluoxetine and norfluoxetine are generated over a concentration range

of 20-200 ng/mL. Overall extraction efficiency of the extraction procedure is found
to be >90% and >75% with correlation coeffs. of 0.997 and 0.993 for fluoxetine and norfluoxetine, resp.
ST fluoxetine norfluoxetine detn blood **gas** chromatog
IT Blood analysis
(fluoxetine and norfluoxetine determination in human, by **gas** chromatog.)
IT 54910-89-3, Fluoxetine **83891-03-6**, Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in human blood by **gas** chromatog.)

L7 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:12289 CAPLUS
DN 114:12289
ED Entered STN: 12 Jan 1991
TI Capillary supercritical fluid chromatography of aliphatic amines. Studies on the selectivity and symmetry with three different columns using carbon dioxide or nitrous oxide as mobile phase
AU Gyllenhaal, Olle; Vessman, Joergen
CS Dep. Anal. Chem., AB Haessle, Moelndal, S-431 83, Swed.
SO Journal of Chromatography (1990), 516(2), 415-26
CODEN: JOCRAM; ISSN: 0021-9673
DT Journal
LA English
CC 64-3 (Pharmaceutical Analysis)
AB The supercrit. fluid chromatog. of intact aliphatic amines with different columns is described. One group of amines was based on N,N-dimethyl-n-octylamine and related primary and secondary amines, and the other on the amino alc. metoprolol and several of its analogs. Columns with 3 phases were investigated, one non-polar coated with 5% Ph Me polysiloxane and two more polar with 25% cyanopropyl methylphenyl polysiloxane and Carbowax 20M. Generally, equal molar amts. were injected under splitless conditions and the peak symmetry was recorded. The system with the non-polar silicone phase was more inert, followed by the wax-phase column. The cyanopropyl column gave severe peak tailing although it was loaded with five times more of the amines than the other columns. The selectivity was investigated and was found higher with the two polar columns. Both showed a marked increase in the retention of amines with free hydrogens. With N2O the selectivity was almost the same as that with CO2 as mobile phase. The nature of the flame ionization detector changed, however, giving a neg. baseline drift on pressure programming. An interesting conclusion is that the amines are chromatographed as such with CO2 as the mobile phase.
ST capillary supercrit **gas** chromatog amine
IT Pharmaceutical analysis
(capillary supercrit. **gas** chromatog. of aliphatic amines in)
IT Siloxanes and Silicones, uses and miscellaneous
RL: USES (Uses)
(Me Ph, column, capillary supercrit. **gas** chromatog., for aliphatic amines)
IT Amines, analysis
RL: ANT (Analyte); ANST (Analytical study)
(aliphatic, **gas** chromatog. of, capillary supercrit., columns and mobile phase effect on)
IT Siloxanes and Silicones, uses and miscellaneous
RL: USES (Uses)
(cyanopropyl Me Ph, column, capillary supercrit. **gas** chromatog., for aliphatic amines)
IT Chromatography, **gas**
(supercrit., of aliphatic amine drugs)
IT Chromatographs, **gas**
(supercrit., columns, for aliphatic amine drugs)

IT 56592-21-3, 20M
RL: ANST (Analytical study)
(column, capillary supercrit. **gas** chromatog., for aliphatic amines)
IT 102-82-9, Tributylamine 111-86-4, n-Octylamine 143-16-8, Di-n-hexylamine 2439-54-5, N-Methyl-n-octylamine 7378-99-6, N,N-Dimethyl-n-octylamine 51384-51-1 **74027-60-4**, H 98/52 109632-08-8, H 173/09 109632-10-2, H 105/29 130918-92-2 130918-93-3, H 170/64 130942-36-8, H 170/69
RL: ANT (Analyte); ANST (Analytical study)
(**gas** chromatog. of, capillary supercrit., columns and mobile phase effect on)
IT 124-38-9, Carbon dioxide, uses and miscellaneous 10024-97-2, Nitrous oxide, uses and miscellaneous
RL: USES (Uses)
(mobile phase, for capillary supercrit. **gas** chromatog. of aliphatic amines)

L7 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:588899 CAPLUS
DN 111:188899
ED Entered STN: 25 Nov 1989
TI Fluoxetine overdose: a case report
AU Rohrig, Timothy P.; Prouty, Richard W.
CS Off. Chief Med. Examiner, Oklahoma City, OK, 73117, USA
SO Journal of Analytical Toxicology (1989), 13(5), 305-7
CODEN: JATOD3; ISSN: 0146-4760
DT Journal
LA English
CC 4-2 (Toxicology)
Section cross-reference(s): 1
AB A fatality due to the ingestion of fluoxetine and ethanol is reported. Quantitation of the drug and its active normetabolite was accomplished by **gas** chromatog. with a flame-ionization detector. Identification of the compds. was performed by **gas** chromatog./mass spectrometry. Tissue distribution of fluoxetine and norfluoxetine, as well as anal. details, is presented.
ST forensic fluoxetine ethanol; alc fluoxetine overdose human
IT Legal chemistry and medicine
(ethanol and fluoxetine overdose in)
IT Poisoning
(from fluoxetine, of human)
IT **83891-03-6**, Norfluoxetine
RL: BIOL (Biological study)
(fluoxetine metabolite, tissue distribution of, in human, forensic)
IT 54910-89-3, Fluoxetine
RL: BIOL (Biological study)
(poisoning from ethanol and, in human)
IT 64-17-5, Ethanol, biological studies
RL: BIOL (Biological study)
(poisoning from fluoxetine and, in human)

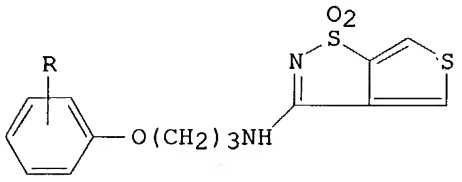
L7 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:526348 CAPLUS
DN 111:126348
ED Entered STN: 14 Oct 1989
TI A single-step extraction for screening whole blood for basic drugs by capillary GC/NPD
AU Cox, Robert A.; Crifasi, Joseph A.; Dickey, Ralph E.; Ketzler, Steven C.; Pshak, Gary L.
CS Dep. Lab. Med., Mem. Med. Cent., Springfield, IL, 62781, USA
SO Journal of Analytical Toxicology (1989), 13(4), 224-8
CODEN: JATOD3; ISSN: 0146-4760

DT Journal
LA English
CC 1-1 (Pharmacology)
Section cross-reference(s): 4, 64
AB Basic drugs were routinely extracted from whole blood under alkaline conditions into Bu acetate. The extract was injected into a **gas** chromatog. with a N-P detector and a wide-bore cross-linked 50% PhMe silicone capillary column. Absolute and relative retention times were recorded for >100 extracted drug stds. Recovery from the whole blood was determined for some of the more frequently encountered drugs. This 1-step extraction is reliable for general screening and was used routinely in forensic and clin. toxicol. analyses.
ST blood basic drug GC; **gas** chromatog basic drug blood
IT Legal chemistry and medicine
(basic drugs determination in human blood by GC in)
IT Chromatography, **gas**
(of basic drugs in human blood)
IT Pharmaceutical analysis
(of basic drugs in human blood by GC)
IT 50-06-6, Phenobarbital, analysis 50-36-2, Cocaine 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, analysis 51-06-9, Procainamide 51-55-8, Atropine, analysis 52-53-9, Verapamil 54-11-5, Nicotine 56-54-2 57-41-0, Phenytoin 57-42-1, Meperidine 57-43-2, Amobarbital 57-44-3, Barbital 57-53-4, Meprobamate 58-08-2, Caffeine, analysis 58-25-3, Chlordiazepoxide 58-38-8, Prochlorperazine 58-40-2, Promazine 58-55-9, Theophylline, analysis 58-73-1, Diphenhydramine 59-46-1, Procaine 60-80-0 60-87-7, Promethazine 63-12-7, Benzoquinamide 64-04-0, Phenethylamine 68-88-2, Hydroxyzine 69-23-8, Fluphenazine 72-44-6, Methaqualone 72-69-5, Nortriptyline 76-42-6, Oxycodone 76-57-3, Codeine 76-73-3, Secobarbital 76-74-4, Pentobarbital 76-99-3, Methadone 77-10-1, Phencyclidine 77-17-8, Norpethidine 77-21-4, Glutethimide 77-26-9, Butalbital 77-41-8, Methsuximide 77-67-8, Ethosuximide 78-44-4, Carisoprodol 91-81-6, Tripelenamine 94-09-7, Benzocaine 96-88-8, Carbocaine 103-90-2, Acetaminophen 113-92-8 115-38-8, Mephobarbital 117-89-5, Trifluoperazine 122-09-8, Phentermine 125-33-7, Primidone 125-40-6, Butabarbital 125-64-4, Methyprylon 125-71-3, Dextromethorphan 134-49-6 137-58-6, Lidocaine 146-22-5, Nitrazepam 244-63-3, 9H-Pyrido[3,4-b]indole 298-46-4, Carbamazepine 299-42-3 300-62-9, Amphetamine 302-33-0, Proadifen 303-49-1, Clomipramine 303-53-7, Cyclobenzaprine 359-83-1, Pentazocine 396-01-0, Triamterene 438-60-8, Protriptyline 439-14-5, Diazepam 469-21-6, Doxylamine 469-62-5, Propoxyphene 486-84-0, Harmane 523-87-5, Dimenhydrinate 525-66-6, Propranolol 537-46-2, Methamphetamine 604-75-1, Oxazepam 634-03-7, Phendimetrazine 723-46-6 739-71-9, Trimipramine 846-49-1, Lorazepam 846-50-4, Temazepam 963-39-3 1088-11-5, Nordiazepam 1225-56-5, Desmethyldoxepin 1668-19-5, Doxepin 1812-30-2, Bromazepam 1977-10-2, Loxapine 2886-65-9 2955-38-6, Prazepam 3737-09-5, Disopyramide 6740-88-1, Ketamine 7143-09-1, Methylecgonine 7722-15-8, Norchlordiazepoxide 10262-69-8, Maprotiline 14028-44-5, Amoxapine 14838-15-4 17617-23-1, Flurazepam 18323-44-9, Clindamycin 20594-83-6, Nalbuphine 24526-64-5, Nomifensine 32795-44-1, n-Acetylprocainamide 41708-72-9, Tocainide 42399-41-7, Diltiazem 51799-32-7, Propylamphetamine 54910-89-3, Fluoxetine 59467-70-8, Midazolam 66778-36-7, Encainide 66796-40-5, Norpropoxyphene 71387-58-1 **83891-03-6**, Norfluoxetine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood by GC, in humans)
IT 91-84-9, Pyrilamine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood, of humans, by **gas** chromatog.)

L7 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:50594 CAPLUS
DN 110:50594
ED Entered STN: 17 Feb 1989
TI Determination of the β-blocker betaxolol and labeled analoges by **gas** chromatography/mass spectrometry with selected ion monitoring of the α-cleavage fragment (m/z 72)
AU Lee, C. R.; Coste, A. C.; Allen, J.
CS Lab. Etud. Rech. Synthelabo, Bagneux, F-92220, Fr.
SO Biomedical & Environmental Mass Spectrometry (1988), Volume Date 1987, 16(1-12), 387-92
CODEN: BEMSEN; ISSN: 0887-6134
DT Journal
LA English
CC 1-1 (Pharmacology)
Section cross-reference(s): 25
AB Low concns. of betaxolol in canine blood plasma and physiol. buffers were determined by selected ion monitoring of the intense m/z 72 fragment [CH2 = NH-CH(CH3)2]+ formed by electron impact ionization of the O-trimethylsilyl derivative At a mass spectrometric resolution of 3000, fewer potentially interfering peaks were seen than at low resolution There remained a chemical interference, corresponding to 100 pg/sample, which arose during treatment of the samples. This method is more sensitive than previous ones, but it is restricted to situations where the specificity can be controlled. When the m/z fragment was mass-shifted by using betaxolol appropriately labeled with deuterium or 13C, both the interference and the baseline noise were greatly reduced; concns. of labeled betaxolol as low as 10-20 pg/sample can be determined with little difficulty.
ST betaxolol blood **gas** chromatog mass spectrometry
IT Blood analysis
(betaxolol determination in, by **gas** chromatog.-mass spectrometry)
IT 63659-17-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of)
IT 63659-18-7, Betaxolol
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood by **gas** chromatog.-mass spectrometry)
IT **118450-46-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with labeled acetone of)
IT 118450-44-5P 118450-45-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for blood determination of betaxolol by **gas** -chromatog.-mass spectroscopy)
IT 666-52-4, 2-Propanone-1,1,1,3,3,3-d6 7217-25-6, 2-Propanone-1,3-13C2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with amino[[(cyclopropylmethoxy)ethyl]phenoxy]propanol)

L7 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:422887 CAPLUS
DN 109:22887
ED Entered STN: 22 Jul 1988
TI Syntheses and **gastric** acid antisecretory properties of the H2-receptor antagonist N-[3-[3-(1-piperidinylmethyl)phenoxy]propyl]thieno[3,4-d]isothiazol-3-amine 1,1-dioxide and related derivatives
AU Santilli, Arthur A.; Scotese, Anthony C.; Morris, Robert L.; Schiehser, Guy A.; Teller, Daniel M.; Nielsen, Susan T.; Strike, Donald P.
CS Res. Div., Wyeth Lab., Inc., Radnor, PA, 19087, USA
SO Journal of Medicinal Chemistry (1988), 31(7), 1480-6
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal

LA English
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
OS CASREACT 109:22887
GI



I

AB The synthesis and **gastric** acid antisecretory properties of several N-substituted thieno[3,4-d]isothiazol-3-amine 1,1--dioxides and analogs are described. Thieno[3,4-d]isothiazol-3-amine 1,1-dioxides I (R = 3-, 4-piperidinomethyl) showed greater potencies as H2-receptor antagonists (in vitro) than ranitidine. They also had potent **gastric** acid antisecretory activities in vivo, inhibiting basal acid secretion in the rat, histamine-stimulated acid secretion in the dog, and only I (R = 3-piperidinomethyl) had food-stimulated acid secretion in the dog. These were selected for further pharmacol. evaluation.

ST piperidinomethylphenoxypropylthienoisothiazoleamine prepn **gastric** acid antisecretory; thienoisothiazoleamine piperidinomethylphenoxypropyl **gastric** acid antisecretory

IT Stomach, metabolism
(acid secretion by, piperidinyl methylphenoxypropylthienoisothiazoleamine dioxide)

IT 69384-12-9 73278-98-5 **73279-03-5** 86134-46-5 87476-77-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(aminolysis by, of methylthiothienoisothiazole dioxide)

IT 73279-35-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(aminolysis of, with hydrazine)

IT 59337-78-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(aminolysis of, with piperidinylmethylphenoxypropylamine)

IT 59337-86-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(chlorination of, with phosphorus chloride)

IT 15504-60-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with bromopropylphthalamide)

IT 73279-04-6, 3-(1-Piperidinylmethyl)phenol
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with dibromopropene)

IT 5460-29-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with hydroxybenzoylpiperidine)

IT 114033-51-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and acetal cleavage of, aldehyde from)

IT 106871-89-0P 114033-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and aminolysis by, of methylthiothienoisothiazole dioxide)

IT 94662-49-4P 106871-87-8P 114033-46-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and aminolysis of)

IT 106871-88-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and aminolysis of, with hydrazine)
IT 114033-53-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with bromopropoxyphenylmethylpiperidine)
IT 114033-54-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with thienoisothiazoleamine dioxide)
IT 94662-39-2P 94662-51-8P 94662-52-9P 106871-90-3P 106871-91-4P 106871-96-9P 106871-97-0P 114033-47-5P 114033-48-6P 114033-49-7P 114033-55-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and **gastric** acid antisecretory properties of)
IT 94662-48-3P 114033-45-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of)
IT 106871-95-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 114033-52-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, **gastric** acid antisecretory properties and aminolysis of, with piperidine)
IT 100306-68-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, **gastric** acid antisecretory properties and cyclization of)
IT 59337-79-0 59337-94-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfurization of, with phosphorus pentasulfide)

L7 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:464988 CAPLUS
DN 107:64988
ED Entered STN: 21 Aug 1987
TI Recent results in the use of phosgene as a derivatizing reagent prior to **gas** chromatography of amino alcohols
AU Gyllenhaal, Olle; Vessman, Joergen
CS AB Haessle, Moelndal, S-431 83, Swed.
SO Journal of Chromatography (1987), 395, 445-53
CODEN: JOCRAM; ISSN: 0021-9673
DT Journal
LA English
CC 64-3 (Pharmaceutical Analysis)
Section cross-reference(s): 1, 22, 25
OS CASREACT 107:64988
AB Recent kinetic expts. concerning the reaction of $COCl_2$ with the amino alc., metoprolol and different related 1-alkylamino-3-(aryloxy)-2-propanols in CH_2Cl_2 show that the amino group substituent affects the reaction rate to a high degree, whereas the aromatic part is of little importance. The relative rate is lower by a factor of 50 for a tert-butylamino group than for an isopropylamino group. Some new examples of compds. of pharmaceutical interest, ketamine, mefloquine, and tryptamine that undergo ring-closure reaction with $COCl_2$ are also presented.
ST amino alc **gas** chromatog phosgene
IT Pharmaceutical analysis
(amino alc. drugs determination in, by **gas** chromatog., derivatization by phosgene in)
IT Chromatography, **gas**

(of amino alcs., derivatization by phosgene in)

IT Alcohols, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(amino, derivatization of, by reaction with phosgene, for **gas** chromatog. determination)

IT 75-44-5
RL: ANST (Analytical study)
(amino alcs. derivatization by, for **gas** chromatog. determination)

IT 525-66-6, Propranolol 6452-71-7, Oxprenolol 13523-86-9, Pindolol 13655-52-2, Alprenolol 26839-75-8, Timolol 37517-30-9, Acebutolol 51384-51-1, Metoprolol 56392-16-6 62572-91-2, H 119/72 62572-93-4, H 119/68 62572-94-5, H 105/22 **74027-60-4** 80448-17-5 91324-71-9 91324-72-0 95503-98-3 109632-07-7 109632-08-8 109632-10-2 109632-11-3
RL: PROC (Process)
(derivatization of, by reaction with phosgene, for **gas** chromatog. determination)

IT 61-54-1, Tryptamine 6740-88-1, Ketamine 51740-76-2, Organon 6001 53230-10-7, Mefloquine
RL: ANT (Analyte); ANST (Analytical study)
(determination of, by **gas** chromatog., derivatization by phosgene in)

IT 109632-05-5
RL: FORM (Formation, nonpreparative)
(formation of, during ketamine derivatization with phosgene in **gas** chromatog. determination)

IT 109659-09-8
RL: FORM (Formation, nonpreparative)
(formation of, during mefloquine derivatization with phosgene in **gas** chromatog. determination)

IT 17952-82-8
RL: FORM (Formation, nonpreparative)
(formation of, during tryptamine derivatization with phosgene in **gas** chromatog. determination)

L7 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1985:78865 CAPLUS
DN 102:78865
ED Entered STN: 09 Mar 1985
TI Fused heterocyclic compounds
IN Schiehser, Guy Alan; Strike, Donald Peter
PA American Home Products Corp., USA
SO Eur. Pat. Appl., 58 pp.
CODEN: EPXXDW
DT Patent
LA English
IC C07D513-04; A61K031-425; A61K031-445
ICI C07D513-04, C07D333-00, C07D275-00
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 120585	A1	19841003	EP 1984-301026	19840217
	EP 120585	B1	19871216		
	R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE				
	US 4490527	A	19841225	US 1983-468221	19830222
	DK 8302705	A	19840823	DK 1983-2705	19830613
	DK 169255	B1	19940926		
	GB 2137197	A1	19841003	GB 1984-4205	19840217
	GB 2137197	B2	19860702		
	ZA 8401200	A	19850925	ZA 1984-1200	19840217
	AT 31417	E	19880115	AT 1984-301026	19840217
	FI 8400687	A	19840823	FI 1984-687	19840220

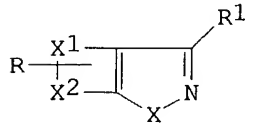
	FI 78107	B	19890228		
	FI 78107	C	19890612		
	AU 8424725	A1	19840830	AU 1984-24725	19840220
	AU 563007	B2	19870625		
	ES 529904	A1	19851116	ES 1984-529904	19840221
	CA 1215709	A1	19861223	CA 1984-447911	19840221
	JP 59193894	A2	19841102	JP 1984-33326	19840222
	JP 05044470	B4	19930706		
PRAI	US 1983-468221		19830222		
	GB 1983-11653		19830428		
	US 1981-330403		19811214		
	US 1982-431879		19820930		
	EP 1984-301026		19840217		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 120585	IC	C07D513-04IC A61K031-425IC A61K031-445
	ICI	C07D513-04, C07D333-00, C07D275-00

OS CASREACT 102:78865

GI



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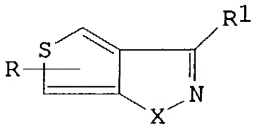

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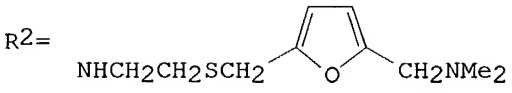
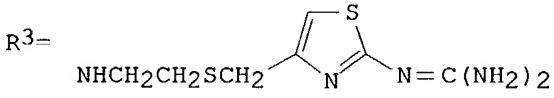
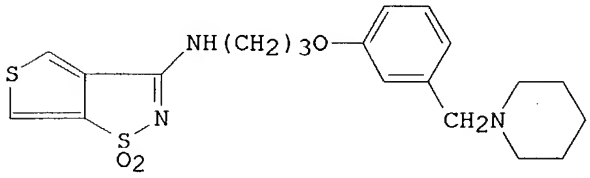






III

AB **Gastric** acid secretion inhibitors, thienothiazole derivs. I and II [R = H, halo, NO2, amino, alkyl, carboxy, etc.; R1 = R2, R3, NH(CH2)nOR4; R4 = (aminomethyl-substituted) Ph; n = 1-4; X = S, SO, SO2, CO; X1 = CH:CH, X2 = S, and vice versa] were prepared Thus thienoisothiazole II (R = H, R1 = SMe, X = SO2), prepared by S-methylation of the corresponding thione, was treated with H2N(CH2)3OC6H4(CH2R5)-3 (R5 = piperidino) to give thienoisothiazole III. III gave 50% inhibition of **gastric** acid secretion in Pavlov-pouch dogs at 0.25 mg/kg orally; at 1 mg/kg III reduced **gastric** acid secretion by 82%.

ST **gastric** secretion inhibitor thienothiazole prepn

IT Stomach, metabolism
(secretion by, inhibitors for, thienothiazoles as)

IT 5460-29-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (piperidinylmethyl)phenol)

IT 73152-41-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with phthalimide)
IT 94662-39-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and methanesulfonic salt formation from)
IT 15433-79-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with aminoethanethiol)
IT 94662-38-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydrazine, ring cleavage by)
IT 66356-53-4P **73279-03-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with thienoisothiazole)
IT 94662-49-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of, with amine derivs.)
IT 94662-50-7P 94662-51-8P 94662-52-9P 94662-53-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and stomach acid secretion inhibition by)
IT 94662-48-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and S-methylation of)
IT 94662-40-5P 94662-41-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 60-23-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminomethylfurylmethanol)
IT 98-00-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dimethylamine)
IT 110-89-4, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxybenzaldehyde)
IT 59337-79-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphorus pentasulfide, thione formation by)
IT 123-08-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with piperidine)
IT 71916-66-0 73278-98-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with thienoisothiazole)

L7 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:558407 CAPLUS
DN 99:158407
ED Entered STN: 12 May 1984
TI Benzo-fused heterocyclic compounds
IN Schiehser, Guy Alan; Strike, Donald Peter
PA American Home Products Corp., USA
SO Eur. Pat. Appl., 81 pp.
CODEN: EPXXDW
DT Patent
LA English
IC C07D275-06; C07D209-50; C07D417-12; A61K031-425; A61K031-40

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

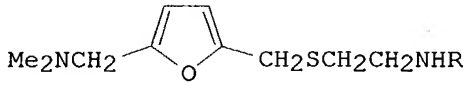
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 81955	A2	19830622	EP 1982-306432	19821203
	EP 81955	A3	19831221		
	EP 81955	B1	19870121		
	R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE				
	GB 2111988	A1	19830713	GB 1982-34543	19821203
	GB 2111988	B2	19850807		
	AT 25082	E	19870215	AT 1982-306432	19821203
	AU 8291406	A1	19830623	AU 1982-91406	19821210
	AU 555220	B2	19860918		
	CA 1185970	A1	19850423	CA 1982-417409	19821210
	DK 8205538	A	19830615	DK 1982-5538	19821213
	ZA 8209150	A	19840725	ZA 1982-9150	19821213
	JP 58116463	A2	19830711	JP 1982-220031	19821214
	JP 03004068	B4	19910122		
PRAI	US 1981-330403		19811214		
	GB 1982-17002		19820611		
	US 1982-431879		19820930		
	EP 1982-306432		19821203		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 81955	IC	C07D275-06IC C07D209-50IC C07D417-12IC A61K031-425IC A61K031-40

GI



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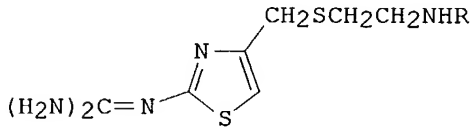

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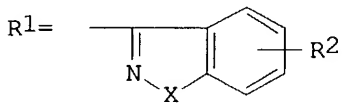


AB H2 antagonists benzoisothiazoles and isoindoles I and II [R = R1; R2 = mono- or dihalo, NO2, cyano, CF3, (un)substituted amino, hydroxy, alkylthio, mercapto, alkyl, alkylsulfonyl, sulfamoyl, Ph; X = SO2, SO, S, CO] and R3O(CH2)nNHR1 [R3 = (un)substituted Ph; n = 1-4] were prepared Thus I (R = H) was treated with ClR1 (R2 = H, X = SO2) to give I (R = R1, R2 = H, X = SO2) (III). III gave 50% inhibition of **gastric** acid output in beagles with a Pavlov pouch at 0.8 mg/kg orally.

ST H2 antagonist benzoisothiazole isoindole prepn; isothiazole benzo H2 antagonist prepn

IT Stomach, metabolism
(secretion by, inhibitors, benzoisothiazoles and isoindoles)

IT 85-41-6 384-45-2 29083-15-6 29083-16-7 29083-17-8 29083-18-9 62473-92-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(chlorination of)

IT 87476-74-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenolysis of)

IT 87477-23-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and methylation of)

IT 87476-73-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, with bromophthalimide)

IT 69384-12-9P 73278-99-6P 81201-16-3P 87476-77-5P 87476-78-6P
87476-79-7P 87476-80-0P 87476-81-1P 87476-82-2P 87476-83-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, with chlorobenzoisothiazole dioxide)

IT 73279-01-3P **73279-03-5P** 86134-47-6P 87476-84-4P
87476-85-5P 87476-86-6P 87476-87-7P 87476-88-8P 87476-89-9P
87476-90-2P 87476-91-3P 87476-92-4P 87476-93-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, with chlorobenzoisothioazole dioxide)

IT 15864-54-7P 87476-59-3P 87476-63-9P 87476-67-3P 87476-69-5P
87476-71-9P 87477-24-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, with piperidinylmethylphenoxypropylamine)

IT 567-19-1P 23661-69-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, with substituted alkylamines)

IT 87476-49-1P 87476-50-4P 87476-51-5P 87476-52-6P 87476-53-7P
87476-55-9P 87476-56-0P 87476-58-2P 87476-60-6P 87476-61-7P
87476-62-8P 87476-64-0P 87476-65-1P 87476-66-2P 87476-75-3P
87476-76-4P 87476-94-6P 87476-95-7P 87476-96-8P 87476-97-9P
87476-98-0P 87476-99-1P 87477-00-7P 87477-01-8P 87477-02-9P
87477-03-0P 87477-04-1P 87477-05-2P 87477-06-3P 87477-07-4P
87477-08-5P 87477-09-6P 87477-10-9P 87477-11-0P 87477-12-1P
87477-13-2P 87477-14-3P 87477-15-4P 87477-16-5P 87477-18-7P
87477-19-8P 87477-20-1P 87477-21-2P 87477-22-3P 87491-64-3P
87491-65-4P 87491-66-5P 87491-67-6P 87491-68-7P 87491-69-8P
87491-70-1P 87491-71-2P 87491-72-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and stomach acid secretion inhibition activity of)

IT 87476-68-4P 87476-70-8P 87476-72-0P 87477-17-6P 87491-73-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

IT 87476-54-8P 87476-57-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, reduction, and stomach acid secretion inhibition activity of)

IT 66356-53-4 71916-66-0 73278-98-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with chlorinated aryl compds.)

IT 100-83-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with morpholine)

IT 5460-29-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with morpholinomethylphenol)

IT 14121-27-8

RL: RCT (Reactant); RACT (Reactant or reagent)

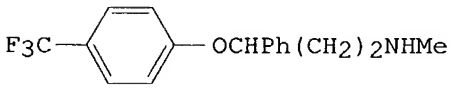
(reaction of, with phosphorus pentasulfide)

IT 15864-53-6 27605-74-9 27605-75-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with piperidinylmethylphenoxypropylamine)

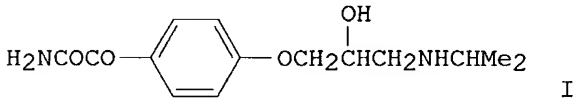
L7 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:81 CAPLUS
DN 98:81
ED Entered STN: 12 May 1984
TI Determination of fluoxetine and norfluoxetine in plasma by **gas** chromatography with electron-capture detection
AU Nash, J. F.; Bopp, R. J.; Carmichael, R. H.; Farid, K. Z.; Lemberger, L.
CS Lilly Res. Lab., Indianapolis, IN, 46285, USA
SO Clinical Chemistry (Washington, DC, United States) (1982), 28(10), 2100-2
CODEN: CLCHAU; ISSN: 0009-9147
DT Journal
LA English
CC 1-1 (Pharmacology)
GI



I

AB The **gas**-chromatog. method for assay of fluoxetine (I) [54910-89-3] and norfluoxetine [**83891-03-6**] in human plasma involves extraction of the drugs and use of a 63Ni electron-capture detector. The organ/methane carrier **gas** flow was 40mL/min. The injector, detector, and column temps. were 250, 300, and 190°, resp. The linear range of detection is 25 to 800 μg/L for each drug. Overall precision (CV) in the concentration range of 10 to 100 μg/L for both drugs was approx. 10%. Accuracy (relative error) in the same concentration range was approx. +10%. None of the commonly prescribed antidepressants or tranquilizers interfered with the assay.
ST fluoxetine norfluoxetine detn blood; **gas** chromatog fluoxetine norfluoxetine
IT Blood analysis
(fluoxetine and norfluoxetine determination in human, by **gas** chromatog.)
IT **83891-03-6**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood of humans by **gas** chromatog., as fluoxetine metabolite)
IT 54910-89-3
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood of humans by **gas** chromatog., in presence of desmethyl metabolite)

L7 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1982:154993 CAPLUS
DN 96:154993
ED Entered STN: 12 May 1984
TI Studies on the metabolism of atenolol. Characterization and determination of a new urinary metabolite in the rat
AU Matsuki, Yasuhiko; Ito, Tomiharu; Komatsu, Sakae; Nambara, Toshio
CS Food Drug Saf. Cent., Hatano Res. Inst., Kanagawa, 257, Japan
SO Chemical & Pharmaceutical Bulletin (1982), 30(1), 196-201
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
CC 1-2 (Pharmacology)
Section cross-reference(s): 25
GI



I

AB A new urinary metabolite of atenolol [29122-68-7] in the rat was characterized and isolated. The metabolite, 4-(2-hydroxy-3-isopropylaminopropoxy)phenylglyoxylic acid amide (I) [74908-93-3], represented 1.04% of the total dose of atenolol administered. A **gas** chromatog. method for the determination of I in urine is presented.

ST atenolol metabolite urine; **gas** chromatog atenolol metabolite urine

IT Urine analysis
(atenolol metabolite determination in, by **gas** chromatog.)

IT 29122-68-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, urinary metabolite determination in)

IT 68758-68-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidation of)

IT 70080-54-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of)

IT 74908-93-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and determination of, in urine, as atenolol metabolite)

IT **81346-71-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with acetone)

IT 81346-70-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with isopropylamine)

IT 29122-69-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reductive amination of)

IT 81346-72-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 17194-82-0 81346-69-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with epichlorohydrin)

L7 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1982:35271 CAPLUS
DN 96:35271
ED Entered STN: 12 May 1984
TI Heterocyclic derivatives and pharmaceutical compositions containing them
IN Clitherow, John Watson; Bradshaw, John; Mackinnon, John Wilson MacFarla; Judd, Duncan Bruce; Bays, David Edmund; Hayes, Roger; Pearce, Andrew
PA Glaxo Group Ltd., UK
SO Fr. Demande, 94 pp.
CODEN: FRXXBL
DT Patent
LA French

IC C07D249-14; A61K031-41
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2477150	A1	19810904	FR 1981-3847	19810226
	FR 2477150	B1	19840316		
	CH 655104	A	19860327	CH 1981-1288	19810226
	BE 887730	A1	19810827	BE 1981-203963	19810227
	SE 8101311	A	19810829	SE 1981-1311	19810227
	SE 448233	B	19870202		
	SE 448233	C	19870611		
	FI 8100619	A	19810829	FI 1981-619	19810227
	FI 76076	B	19880531		
	FI 76076	C	19880909		
	DK 8100906	A	19810829	DK 1981-906	19810227
	NO 8100681	A	19810831	NO 1981-681	19810227
	AU 8167933	A1	19810903	AU 1981-67933	19810227
	AU 544357	B2	19850523		
	NL 8100979	A	19811001	NL 1981-979	19810227
	NL 186812	B	19901001		
	NL 186812	C	19910301		
	GB 2075007	A	19811111	GB 1981-6314	19810227
	GB 2075007	B2	19830713		
	DE 3107628	A1	19820401	DE 1981-3107628	19810227
	DE 3107628	C2	19910314		
	ES 499931	A1	19820601	ES 1981-499931	19810227
	ZA 8101331	A	19821027	ZA 1981-1331	19810227
	CA 1158649	A1	19831213	CA 1981-371889	19810227
	AT 8100939	A	19850915	AT 1981-939	19810227
	AT 380240	B	19860425		
	IL 62229	A1	19871030	IL 1981-62229	19810227
	JP 56147777	A2	19811116	JP 1981-29293	19810228
	JP 03038269	B4	19910610		
	ES 509669	A1	19830316	ES 1982-509669	19820216
	ES 518305	A1	19840616	ES 1982-518305	19821216
	US 4670448	A	19870602	US 1983-465616	19830210
	ES 530741	A1	19850701	ES 1984-530741	19840316
	AT 8401510	A	19880815	AT 1984-1510	19840508
	AT 387774	B	19890310		
	JP 01052763	A2	19890228	JP 1988-47352	19880229
	NL 8802221	A	19890102	NL 1988-2221	19880909
PRAI	GB 1980-6806		19800228		
	AT 1981-939		19810227		
	NL 1981-979		19810227		
	US 1981-238688		19810227		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
FR 2477150	IC	C07D249-14IC A61K031-41

OS CASREACT 96:35271
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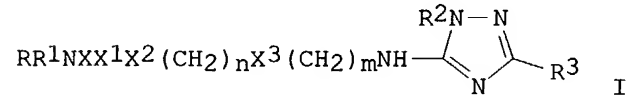

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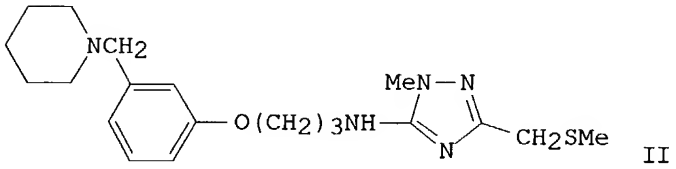

II

AB Triazoles I (X = alkylene; X1 = optionally substituted furyl, thienyl, C6H4; X2, X3 = O, S, NH, bond; m = 2-5; n = 0-3; R = optionally substituted alkyl, cycloalkyl; R1 = H, alkyl; NRR1 = heterocyclic; R2 = H, optionally substituted alkyl; R3 = substituted alkyl, alkenyl) were prepared Thus II was obtained by treating PhCH:NNMeC(:NH)SMe with MeSCH2COCl and treating PhCH:NNMeC(SMe):NCOCH2SMe with 3-(3-piperidinomethyl)phenoxypropa namine. II had a **gastric** acid secretion-inhibiting ED50 of <0.7 mg/kg orally in rats.

ST aminotriazole prepn stomach secretion; triazoleamine prepn stomach secretion

IT Stomach, metabolism
(secretion of, inhibition of, by aminotriazole derivs.)

IT 80343-52-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of)

IT 34767-77-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of)

IT 76-05-1, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, with aminoguanidine)

IT 20863-64-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxymethylation of)

IT 24807-56-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)

IT 76955-94-7 76955-99-2 76956-02-0 80343-62-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidation of)

IT 80343-18-6P 80343-30-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of)

IT 31123-19-0P 76955-97-0P 80371-54-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amination of)

IT 80343-20-0P 80343-26-6P 80343-27-7P 80343-28-8P 80343-29-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and aminolysis of)

IT 80343-17-5P 80343-22-2P 80343-23-3P 80343-24-4P 80343-25-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

IT 80343-55-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and deacylation of)

IT 76956-56-4P 80343-36-8P 80343-39-1P 80343-40-4P 80343-44-8P
80343-45-9P 80343-47-1P 80343-51-7P 80343-54-0P 80343-63-1P
80343-64-2P 80343-73-3P 80343-74-4P 80343-77-7P 80343-85-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and **gastric** secretion-inhibiting activity of)

IT 76963-79-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

IT 80343-71-1P 80343-83-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)

IT 80343-04-0P 80343-05-1P 80343-07-3P 80343-08-4P 80343-11-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with amines)

IT 78908-88-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with aminoethanediol)

IT 78908-98-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with aminoethanethiol)

IT 78909-01-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydrazinecarboximidothioate)

IT 78908-82-4P 80343-68-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

IT 78909-09-8P 80343-09-5P 80343-10-8P 80343-13-1P 80343-14-2P
80343-16-4P 80343-19-7P 80343-21-1P 80343-31-3P 80343-32-4P
80343-33-5P 80343-34-6P 80343-35-7P 80343-37-9P 80343-38-0P
80343-41-5P 80343-42-6P 80343-43-7P 80343-46-0P 80343-48-2P
80343-49-3P 80343-50-6P 80343-53-9P 80343-56-2P 80343-57-3P
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80343-89-1P 80343-90-4P 80343-91-5P 80343-92-6P 80343-93-7P
80343-94-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 80343-59-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, dehydration, and **gastric** secretion-inhibiting activity of)

IT 80343-67-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, esterification, and **gastric** secretion-inhibiting activity of)

IT 35600-34-1 76955-76-5 76956-75-7 80343-06-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with amines)

IT 76955-72-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminotriazole)

IT 69340-48-3
RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with aminotriazole derivative)
IT 73279-32-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminotriazolecarboxylate)
IT 156-57-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dimethylaminomethylthiophenemethanol)
IT 5271-67-0 6419-36-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with guanidine derivative)
IT 6780-38-7 10314-06-4 14794-31-1 35928-65-5 38939-83-2 39901-94-5
56841-99-7 66356-53-4 69384-05-0 69384-31-2 72263-17-3
73278-88-3 73278-98-5 **73279-03-5** 78909-09-8 79185-50-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydrazinecarboximidothioate)
IT 73279-04-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with isoindoledione)
IT 58290-51-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with piperidinylmethylphenol)
IT 3641-14-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with piperidinylmethylphenoxybutanal)
IT 80343-70-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with piperidinylmethylphenoxypropanamine)
IT 141-82-2, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with triazolecarboxaldehyde derivative)
IT 5848-24-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with triazolemethanamine)
IT 80343-15-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with trifluoroacetic acid)

L7 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:181197 CAPLUS
DN 92:181197
ED Entered STN: 12 May 1984
TI Triazole compounds
IN Clitherow, John Watson; Bradshaw, John; Mackinnon, John Wilson Macfarlane; Price, Barry John; Martin-Smith, Michael; Judd, Duncan Bruce
PA Glaxo Group Ltd., UK
SO Ger. Offen., 94 pp.
CODEN: GWXXBX
DT Patent
LA German
IC C07D249-14; C07D401-12; C07D405-00; C07D409-00
CC 28-11 (Heterocyclic Compounds (More Than One Hetero Atom))
FAN.CNT 1

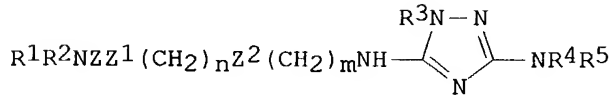
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2917026	A1	19791108	DE 1979-2917026	19790426
	GB 2023133	A	19791228	GB 1979-13730	19790419
	GB 2023133	B2	19820908		
	JP 54160391	A2	19791219	JP 1979-50749	19790424
	JP 03051708	B4	19910807		
	BE 875846	A1	19791025	BE 1979-194830	19790425
	FR 2432511	A1	19800229	FR 1979-10459	19790425
	FR 2432511	B1	19860425		
	CH 647767	A	19850215	CH 1979-3909	19790425

	SE 7903698	A	19791027	SE 1979-3698	19790426
	DK 7901735	A	19791027	DK 1979-1735	19790426
	FI 7901360	A	19791027	FI 1979-1360	19790426
	NO 7901387	A	19791029	NO 1979-1387	19790426
	NL 7903313	A	19791030	NL 1979-3313	19790426
	AU 7946482	A1	19791101	AU 1979-46482	19790426
	AU 531224	B2	19830818		
	ZA 7902021	A	19800625	ZA 1979-2021	19790426
	ES 479988	A1	19800816	ES 1979-479988	19790426
	US 4318913	A	19820309	US 1979-33508	19790426
	CA 1143727	A1	19830329	CA 1979-326446	19790426
	HU 29057	O	19840130	HU 1979-GA1282	19790426
	AT 7903166	A	19840315	AT 1979-3166	19790426
	AT 376212	B	19841025		
	DE 2954639	C2	19900927	DE 1979-2954639	19790426
	IL 57178	A1	19841130	IL 1979-57178	19790430
	ES 488676	A1	19801216	ES 1980-488676	19800216
	ES 488676	A5	19810114		
	ES 488677	A1	19801216	ES 1980-488677	19800216
	ES 488678	A1	19801216	ES 1980-488678	19800216
	AT 8104288	A	19840415	AT 1981-4288	19811006
	AT 376423	B	19841126		
	US 4442110	A	19840410	US 1981-324440	19811124
	AT 8300805	A	19840315	AT 1983-805	19830308
	AT 376213	B	19841025		
	AT 8301279	A	19840315	AT 1983-1279	19830411
	AT 376214	B	19841025		
	US 4764612	A	19880816	US 1986-826832	19860206
PRAI	GB 1978-16468		19780426		
	GB 1978-47689		19781208		
	GB 1979-7422		19790302		
	AT 1979-3166		19790426		
	US 1979-33508		19790426		
	AT 1981-4288		19811006		
	US 1981-324400		19811124		
	US 1983-517509		19830726		

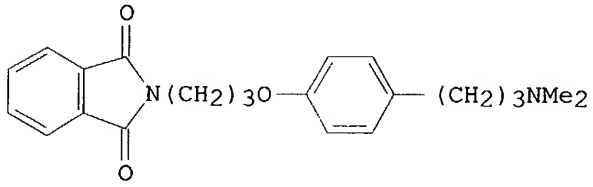
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 2917026	IC	C07D249-14IC C07D401-12IC C07D405-00IC C07D409-00

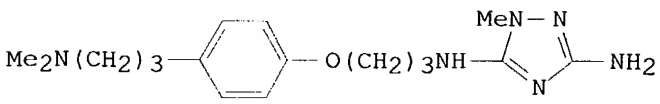
GI



I



II



IV

AB Triazoles I [R1, R2 = H, (cyclo)aliphatic, aralkyl, trifluoroalkyl, alkyl optionally substituted with OH, alkoxy, amino, (di)alkylamino, cycloalkyl; NR1R2 = 5-10 membered heterocyclyl, optionally substituted with ≥1 C1-3 alkyl, OH; R3 = H, alkyl, alkenyl, aralkyl, C ≥2 hydroxyalkyl, alkoxyalkyl, aryl; R4, R5 = H, alkyl optionally substituted with OH or C1-3 alkoxy, alkenyl, aralkyl, heteroalkyl, NR4R5 = 5-7 membered heterocyclyl, R4R5 = :CR8R9 (R8 = aryl, heteroaryl; R9 = H, alkyl); Z = C1-6 alkylene; Z1 = optionally substituted 2,5-furan- or thiophenediyl, C6H4; Z2 = CH2, NR6 (R6 = H, Me), O, S; n = 0, 1, 2; m = 2, 3, 4] and their physiol. acceptable salts, useful as histamine antagonists and inhibitors of hypersecretion of stomach acids (no data) were prepared Thus, stirring 4-Me2N(CH2)3C6H4OH in DMF with NaH 24 h and stirring a further 24 h with N-(3-bromopropyl)phthalimide at 0° gave amino ether II which was hydrazinolyzed in refluxing EtOH 4 h to give 4-H2N(CH2)3OC6H4(CH2)3NMe2 (III). Heating III with PhCH:NNMeC(:NCN)SMe 8 h at 70°/20 mm gave the cyclization product IV.

ST histamine antagonist triazole prepn; **gastric** secretion inhibitor triazole prepn; hydrazinocarboximidothioate cyclization aminopropoxybenzenepropanamine; carboximidothioate hydrazino cyclization amine

IT Stomach, metabolism
(acid secretion by, triazole derivs. inhibition of)

IT 69383-92-2
RL: PROC (Process)
(acetalization of, with ethanediol)

IT 100-83-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with piperidine)

IT 75-07-0, reactions 100-52-7, reactions 123-38-6, reactions 500-22-1 872-85-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with triazolediamine derivative)

IT 79-17-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, with Pr isothiocyanate derivative)

IT 78-81-9 100-46-9, reactions 107-10-8, reactions 107-11-9 108-00-9 108-91-8, reactions 109-73-9, reactions 109-85-3 110-91-8, reactions 111-68-2 141-91-3 626-58-4 694-05-3 1121-92-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, with hydrazinecarboximidamide derivative, triazole derivative by)

IT 2450-71-7 69384-15-2 72158-86-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization of, with hydrazinecarboximidothioate ester)

IT 73279-24-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with benzaldehyde)

IT 73279-11-5P 73279-34-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)

IT 73279-25-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with (aminopropoxy)benzenemethanamine derivative)

IT 73278-89-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with amines)

IT 73279-29-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with aminoguanidine)
IT 73278-87-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with aminopropanol or derivative)
IT 73279-15-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with cyanoguanidine)
IT 73279-14-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with diamine)
IT 66357-42-4P 73279-12-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with hydrazine)
IT 73278-92-9P **73278-96-3P** **73278-97-4P** 73278-98-5P
73278-99-6P 73279-00-2P 73279-01-3P **73279-03-5P**
73279-05-7P 73279-09-1P 73279-19-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with hydrazinothiocarboximidate derivative)
IT 73279-16-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, with methylhydrazine)
IT 73278-93-0P 73278-95-2P 73279-33-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrazinolysis of)
IT 73279-31-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
IT 73279-10-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with (aminomethyl)furanmethanol)
IT 73278-91-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with cysteamine hydrochloride)
IT 73279-32-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with diaminotriazole)
IT 73278-85-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with dimethylmethylenammonium chloride)
IT 73279-35-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydrazine)
IT 72127-23-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydrazine or derivative)
IT 73279-07-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with piperidine)

IT 73279-08-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with potassium phthalimide)

IT 73279-21-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with pyrrolidine)

IT 73279-30-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with semicarbazide)

IT 73278-88-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with thiocarboximidate derivative)

IT 73278-22-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of)

IT 73278-90-7P 73279-20-6P 73279-22-8P 73279-23-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of, with lithium aluminum hydride)

IT 73278-50-9P 73279-17-1P 73279-18-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of, with sodium borohydride)

IT 73278-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N,N-dimethylation of)

IT 73279-27-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-alkylation of piperidine by)

IT 73279-04-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and O-alkylation of)

IT 73278-23-6 73278-24-7 73278-25-8 73278-26-9 73278-27-0
73278-28-1 73278-29-2 73278-30-5 73278-31-6 73278-32-7
73278-33-8 73278-34-9 73278-35-0 73278-36-1 73278-37-2
73278-38-3 73278-39-4 73278-40-7 73278-41-8 73278-42-9
73278-43-0 73278-44-1 73278-46-3 73278-47-4 73278-48-5
73278-49-6 73278-50-9 73278-51-0 73278-52-1 73278-53-2
73278-55-4 73278-56-5 73278-57-6 73278-58-7 73278-59-8
73278-60-1 73278-61-2 73278-62-3 73278-63-4 73278-64-5
73278-65-6 73278-66-7 73278-67-8 73278-68-9 73278-69-0
73278-70-3 73278-71-4 73278-72-5 73278-73-6 73278-74-7
73278-75-8 73278-76-9 73278-77-0 73278-78-1 73278-79-2
73278-80-5 73278-81-6 73278-82-7 73278-83-8 73278-84-9
73278-86-1 73287-83-9 73287-84-0 73424-05-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as histamine antagonist)

IT 73279-02-4P 73279-06-8P 73279-26-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 156-57-0
RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, with (piperidinylmethyl)benzenemethanol)
IT 73279-13-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (piperidinylmethyl)phenoxypropanamine derivative)
IT 15433-79-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with aminobutanol)
IT 1074-82-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with anilinium salt)
IT 1455-77-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with butanal derivative)
IT 109-84-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carbonimidodithioate ester)
IT 123-75-1, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chlorotriazolamine derivative)
IT 60-34-4 13466-29-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cyanocarbonimidodithioate ester)
IT 30354-18-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with furan derivative)
IT 13325-10-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with furanmethanol derivative)
IT 36415-21-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydrazinecarboximidothioate derivative)
IT 156-87-6 5382-16-1 69384-05-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydrazinocarboximidate derivative)
IT 66356-53-4 66356-58-9 66356-77-2 69340-29-0 69340-32-5
69384-12-9 72126-72-8 72158-79-3 72158-81-7 72158-84-0
72158-85-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydrazinocarboximidothioate ester)
IT 73279-28-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosphorus tribromide)
IT 110-68-9 111-49-9 753-90-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phthalimide derivative)
IT 73279-02-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with piperidine)
IT 4819-75-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with triazolamine derivative)
IT 110-89-4P, preparation 10191-60-3
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(reactions of)
IT 51-45-6, biological studies
RL: USES (Uses)
(receptors, triazole derivs. effect on)
IT 1129-28-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation of piperidine)
IT 33322-60-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation of, with (bromopropyl)phthalimide)

IT 5460-29-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(O-alkylation of (aminoalkyl)phenols)
IT 5332-06-9 5394-18-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(O-alkylation of (piperidinylmethyl)phenol by)
IT 123-08-0 539-15-1 73278-94-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(O-alkylation of, with (bromopropyl)phthalimide)

L7 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1979:121258 CAPLUS
DN 90:121258
ED Entered STN: 12 May 1984
TI Aminoalkylbenzene derivatives
IN Price, Barry John; Clitherow, John Watson; Bradshaw, John; Martin-Smith, Michael
PA Allen and Hanburys Ltd., UK
SO Ger. Offen., 56 pp.
CODEN: GWXXBX
DT Patent
LA German
IC C07C093-00
CC 25-21 (Noncondensed Aromatic Compounds)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2821410	A1	19781130	DE 1978-2821410	19780516
	GB 1604674	A	19811216	GB 1977-20660	19770517
	ZA 7802649	A	19790530	ZA 1978-2649	19780509
	FI 7801490	A	19781118	FI 1978-1490	19780511
	AU 7836067	A1	19791115	AU 1978-36067	19780512
	AU 523496	B2	19820729		
	BE 867106	A1	19781116	BE 1978-187722	19780516
	DK 7802148	A	19781118	DK 1978-2148	19780516
	SE 7805591	A	19781118	SE 1978-5591	19780516
	SE 443558	B	19860303		
	SE 443558	C	19861009		
	CH 643238	A	19840530	CH 1978-5315	19780516
	NL 7805344	A	19781121	NL 1978-5344	19780517
	JP 53149936	A2	19781227	JP 1978-58706	19780517
	JP 01012744	B4	19890302		
	FR 2401135	A1	19790323	FR 1978-14594	19780517
	FR 2401135	B1	19830819		
	ES 469953	A1	19790916	ES 1978-469953	19780517
	FR 2398718	A1	19790223	FR 1978-28239	19781003
	FR 2398718	B1	19821015		
	AU 541144	B2	19841220	AU 1982-84117	19820525
	AU 8284117	A1	19820826		
	CH 643233	A	19840530	CH 1982-7491	19821221
	JP 63054343	A2	19880308	JP 1986-288643	19861203
	JP 01053862	B4	19891115		
	US 5021429	A	19910604	US 1986-944217	19861222
PRAI	GB 1977-20660		19770517		
	GB 1977-40129		19770927		
	GB 1978-17444		19780503		
	CH 1978-5315		19780516		
	US 1978-906619		19780516		
	US 1980-200607		19801024		
	US 1983-502674		19830609		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

DE 2821410 IC C07C093-00
OS CASREACT 90:121258
AB RR1NQC6H4(CH2)nQ1(CH2)mNHC(X)NHR2 (I; R, R1 independently = H, alkyl, alkenyl, cycloalkyl, aralkyl, or RR1N = heterocyclyl; R2 = H, alkyl, alkenyl, alkoxyalkyl; Q = C1-6-alkylene; Q1 = O, S, CH2 or NR3, R3 = H or alkyl; X = O, S, NR4, CHR5, where R4 = H, NO2, CN, alkyl, aryl, arylslfonyl or alkylsulfonyl and R5 = NO2, alkylsulfonyl or arylsulfonyl; m = 2-4; n = 0-2), which inhibited allergy and **gastric** juice secretion (no data), were prepared Thus, 3-H2N(CH2)3OC6H4CH2NMe2 was refluxed 4 h in EtOH with MeSO2N:C(SMe)2, then MeNH2 was added and the mixture refluxed 1.5 h to give 3-Me2NCH2C6H4O(CH2)3NHC(:NSO2Me)NHMe.
ST allergy inhibitor aminoalkylbenzene; **gastric** secretion inhibitor aminoalkylbenzene; aminoalkylbenzene allergy inhibitor prepn; benzene aminoalkyl ureidoalkyl; urea aminoalkylaralkyl; amidine aminoalkylaralkyl; guanidine aminoalkylaralkyl
IT Stomach, metabolism
(secretion by, inhibition of, by aminoalkylbenzenes)
IT Allergy
(inhibitors, aminoalkylbenzene derivs.)
IT 556-61-6 624-83-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction of, with diamine)
IT 107-13-1, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(addition reaction of, with hydroxybenzaldehyde)
IT 90-02-8, reactions 123-08-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (bromoalkyl)phthalimides)
IT 103-87-7 60760-04-5 69384-63-0 69384-64-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (haloalkyl)phthalimides)
IT 74-89-5, reactions 124-40-3, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with Me (chloroformyl)benzoate)
IT 75-04-7, reactions 109-85-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with Me thioacetimidate derivative)
IT 69384-65-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with [(dimethylamino)methyl]phenol)
IT 5394-18-3 5460-29-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with aminophenols)
IT 2986-25-6 5848-24-8 22907-04-6 69340-48-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with diamines)
IT 69384-66-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with dimethylamine)
IT 13623-94-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with ethylamine derivative)
IT 56030-23-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation-condensation of, with ethanolic dimethylamine)
IT 3441-03-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of)
IT 69383-74-0P 69383-76-2P 69383-78-4P 69383-80-8P 69383-81-9P
69383-82-0P 69383-83-1P 69383-85-3P 69383-86-4P 69383-88-6P
69383-90-0P 69383-91-1P 69383-95-5P 69383-96-6P 69384-00-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation and ammonolysis of)

IT 69383-99-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation with (bromopropyl)phthalimide)

IT 69384-04-9P 69384-05-0P **69384-07-2P** 69384-08-3P
69384-10-7P 69384-11-8P 69384-13-0P 69384-15-2P 69384-16-3P
69384-17-4P 69384-18-5P 69384-19-6P 69384-20-9P 69384-21-0P
69384-22-1P 69384-23-2P 69384-24-3P 69384-26-5P 69384-27-6P
69384-31-2P 69497-57-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation with Me methylnitrothioacetimidate)

IT 69383-70-6P 69383-72-8P 69383-73-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation with amines)

IT 69383-92-2P 69383-93-3P 69383-94-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation with dimethylamine)

IT 69384-58-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation with methoxyethylamine)

IT 69384-01-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation with methylamine)

IT 69384-02-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)

IT 69384-29-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with tosyl chloride and potassium cyanide)

IT 69384-28-7P 69384-30-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and reduction by lithium aluminum hydride)

IT 23668-00-0P 69383-71-7P 69383-98-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

IT 69383-75-1P 69383-77-3P 69383-79-5P 69383-87-5P 69383-89-7P
69383-97-7P 69384-14-1P 69384-25-4P 69384-32-3P 69384-33-4P
69384-34-5P 69384-35-6P 69384-36-7P 69384-37-8P 69384-38-9P
69384-39-0P 69384-40-3P 69384-41-4P 69384-42-5P 69384-43-6P
69384-44-7P 69384-45-8P 69384-46-9P 69384-47-0P 69384-48-1P
69384-49-2P 69384-51-6P 69384-52-7P 69384-53-8P 69384-54-9P
69384-55-0P 69384-56-1P 69384-57-2P 69384-59-4P 69384-60-7P
69384-61-8P 69384-62-9P 69384-67-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 151-50-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (chloropropyl)[(dimethylamino)methyl]benzene)

IT 156-57-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with [(dimethylamino)methyl]benzenemethanol)

IT 1877-71-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with thionyl chloride)

IT 123-75-1, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction-condensation of hydroxybenzaldehyde with)

IT 100-83-4
RL: RCT (Reactant); RACT (Reactant or reagent)

(reduction-condensation of pyrrolidine with)

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	163.60	320.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-34.30	-34.30

STN INTERNATIONAL LOGOFF AT 10:55:27 ON 15 SEP 2004